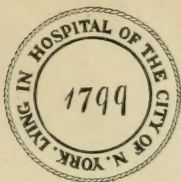




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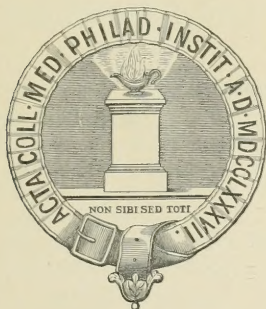


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TRANSACTIONS  
OF THE  
COLLEGE OF PHYSICIANS  
OF  
PHILADELPHIA.

THIRD SERIES.  
VOLUME THE TWENTY-THIRD.



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1901.

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The present volume of TRANSACTIONS contains the papers read before the College from January, 1901, to December, 1901, inclusive.

The Committee of Publication thinks it proper to say that the College holds itself in no way responsible for the statements, reasonings, or opinions set forth in the various papers published in its TRANSACTIONS.

EDITED BY

WILLIAM ZENTMAYER.

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DORNAN, PRINTER.

# COLLEGE OF PHYSICIANS OF PHILADELPHIA.

1901.

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*Clerk*, S. McC. HAMILL, M.D.



LIST  
OF THE  
PRESIDENTS OF THE COLLEGE FROM THE TIME OF ITS  
INSTITUTION.

---

ELECTED

1787	JOHN REDMAN
1805	WILLIAM SHIPPEN
1809	ADAM KUHN
1818	THOMAS PARKE
1835	THOMAS C. JAMES *
1835	THOMAS T. HEWSON
1848	GEORGE B. WOOD
1879	W. S. W. RUSCHENBERGER
1883	ALFRED STILLÉ
1884	SAMUEL LEWIS †
1884	J. M. DA COSTA
1886	S. WEIR MITCHELL
1889	D. HAYES AGNEW
1892	S. WEIR MITCHELL
1895	J. M. DA COSTA
1898	JOHN ASHHURST, JR.
1900	W. W. KEEN, M.D.

\* Died four months after his election.

† Resigned on account of ill-health.



FELLOWS  
OF THE  
COLLEGE OF PHYSICIANS OF PHILADELPHIA.

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DECEMBER, 1901.

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\* Non-resident Fellows.

† Fellows who have commuted dues.

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ELECTED

- \*1883. ABBOT, GRIFFITH E., Ph.D., M.D., Washington, D. C.
- 1892. ABBOTT, ALEX. C., M.D., Professor of Hygiene and Bacteriology, and Director of the Laboratory of Hygiene in the University of Pennsylvania.
- 1876. ALISON, ROBERT H., M.D., Attending Physician to the Bryn Mawr Hospital.
- 1873. ALLIS, OSCAR H., M.D., Surgeon to the Presbyterian Hospital.
- 1896. ALLYN, HERMAN B., M.D., Instructor in Physical Diagnosis in the University of Pennsylvania; Physician to the Philadelphia Hospital; Clinical Professor of Medicine in the Woman's Medical College of Pennsylvania.
- 1888. ANDERS, JAMES M., M.D., LL.D., Professor of the Theory and Practice of Medicine and Clinical Medicine in the Medico-Chirurgical College; Physician to the Medico-Chirurgical and Samaritan Hospitals.
- 1869. ANDREWS, T. HOLLINGSWORTH, M.D., Medical Director of the Bureau of Police and Fire, and Commandant of the Philadelphia Emergency Corps of the Department of Public Safety.
- 1896. ANGNEY, WILLIAM M., M.D., Physician to the House of Mercy (Home for Male Consumptives); Consulting Physician to the Hospital for Diseases of the Lungs, at Chestnut Hill.
- \*1882. ASHBRIDGE, RICHARD, M.D., West Whiteland, Pa.

## ELECTED

1893. ASHTON, THOMAS G., M.D., Physician to the Philadelphia Hospital; Assistant Physician to the Jefferson Medical College Hospital; Clinical Professor of Medicine in the Woman's Medical College of Pennsylvania.
1857. ATLEE, WALTER FRANKLIN, A.M., M.D., Corresponding Member of *La Société des Sciences Médicales de Lyons*; Consulting Surgeon to St. Luke's Hospital, Bethlehem; Visiting Physician to the Preston Retreat.
1852. BACHE, THOMAS HEWSON, M.D.
1883. BAER, BENJAMIN F., M.D., Professor of Gynecology in the Philadelphia Polyclinic.
- †1892. BAKER, GEORGE FALES, B.S., M.D.
1879. BAKER, WASHINGTON H., M.D., Obstetrician to the Maternity Hospital.
1889. BALDY, JOHN MONTGOMERY, M.D., Professor of Gynecology in the Philadelphia Polyclinic; Surgeon to the Gyneccean Hospital and to the Gynecological Out-patient Department of the Pennsylvania Hospital; Consulting Surgeon to the Frederick Douglass Memorial Hospital.
1898. BALLIET, TILGHMAN M., A.M., M.D., Professor of Therapeutics at Dartmouth College, Hanover, N. H.; Physician to the Old Man's Home.
1880. BARTHOLOW, ROBERTS, M.D., Professor (Emeritus) of *Materia Medica*, General Therapeutics and Hygiene in the Jefferson Medical College.
1894. BARTON, JAMES M., M.D., Surgeon to the Jefferson Medical College Hospital and to the Philadelphia Hospital.
1883. BAUM, CHARLES, A.M., M.D., Ph.D.
1883. BEATES, HENRY, M.D.
1860. BENNER, HENRY D., M.D.
1874. BENNETT, W. H., M.D., Physician-in-charge to the Seashore Home for Invalid Children, and to the Seaside House for Invalid Women, Atlantic City; formerly Physician to the Episcopal Hospital, and Physician-in-charge to St. Christopher's Hospital for Children.
1896. BEYEA, HENRY D., M.D., Instructor in Gynecology and Assistant Demonstrator of Obstetrics in the University of Pennsylvania; Assistant Surgeon to the Gyneccean Hospital.

## ELECTED

- †1884. BIDDLE, ALEXANDER W., M.D.  
 1884. BIDDLE, THOMAS, M.D.
- \*1866. BLACK, J. J., M.D., New Castle, Del.
1894. BLISS, ARTHUR AMES, M.D., Laryngologist and Aurist to the German Hospital; Consulting Laryngologist to the Pennsylvania Institution for the Deaf and Dumb.
- \*1867. BOARDMAN, CHARLES H., M.D., Evanston, Illinois.
1894. BOCHROCH, MAX H., M.D., Instructor in Electro-therapeutics and Chief Clinical Assistant in the Nervous Department of the Jefferson Medical College Hospital; Neurologist to the Out-patient Department of St. Joseph's Hospital.
1896. BOGER, JOHN A., M.D., Surgeon to St. Mary's and the Samaritan Hospitals; Surgeon to the Dispensary of the Episcopal Hospital.
1891. BOYD, GEORGE M., M.D., Clinical Professor of Obstetrics in the Medico-Chirurgical College; Physician to the Philadelphia Lying-in Charity Hospital and Nurse School.
- †1884. BRADFORD, T. HEWSON, M.D.
1856. BRINTON, JOHN H., M.D., LL.D., Professor of the Practice of Surgery and of Clinical Surgery in the Jefferson Medical College; Consulting Surgeon to St. Joseph's Hospital and to the Southwestern Hospital of Philadelphia.
1891. BRINTON, LEWIS, M.D., Visiting Physician to the Nervous Department of the Howard Hospital.
1900. BRINTON, WARD, M.D., Demonstrator of Physical Diagnosis in the Jefferson Medical College; Physician to the Dispensary of St. Christopher's Hospital for Children; Assistant in the Medical Dispensary of the Jefferson Medical College Hospital.
1887. BRUBAKER, ALBERT P., M.D., Professor of Physiology in the Pennsylvania College of Dental Surgery; Adjunct Professor of Physiology and Hygiene in the Jefferson Medical College; Lecturer on Anatomy and Physiology in the Drexel Institute.
- \*1890. BRUSH, EDWARD N., M.D., Medical Superintendent of the Shepherd and Enoch Pratt Hospital, Towson, Md.
- \*1851. BULLOCK, WILLIAM R., M.D., Wilmington, Del.
1870. BURNETT, CHARLES H., M.D., Professor (Emeritus) of Otology in the Philadelphia Polyclinic; Clinical Professor of Otology

## FELLOWS

- in the Woman's Medical College; Aural Surgeon to the Presbyterian Hospital; Consulting Aurist to the Pennsylvania Institution for the Deaf and Dumb.
1892. BURR, CHARLES W., M.D., Professor of Mental Diseases in the University of Pennsylvania; Neurologist to the Philadelphia Hospital.
1886. CADWALADER, CHARLES E., M.D.
1895. CARPENTER, JOHN T., M.D.
- \*1897. CARTER, WILLIAM S., M.D., Professor of Physiology in the University of Texas.
1892. CATTELL, HENRY W., A.M., M.D., Editor of the *International Clinics*.
- \*1892. CERNA, DAVID, M.D., Ph.D., Galveston, Texas, Demonstrator of Physiology in the Department of Medicine of the University of Texas; Corresponding Fellow of the Sociedad Española de Higiene of Madrid.
1900. CHANCE, BURTON KOLLOCK, M.D., Assistant Surgeon to the Wills Eye Hospital.
1885. CHAPIN, JOHN B., M.D., Physician-in-Chief to the Pennsylvania Hospital for the Insane.
1880. CHAPMAN, HENRY C., M.D., Professor of the Institutes of Medicine and of Medical Jurisprudence in the Jefferson Medical College.
1900. CHASE, ROBERT HOWLAND, A.M., M.D., Superintendent of the Friends' Asylum for the Insane.
1868. CHESTON, D. MURRAY, M.D.
1897. CHESTON, RADCLIFFE, M.D.
1899. CLARK, JOHN G., M.D., Professor of Gynecology in the University of Pennsylvania; Gynecologist-in-Chief to the University Hospital.
1897. CLAXTON, CHARLES, A.M., M.D.
1872. CLEEMANN, RICHARD A., M.D.
1896. CLEVELAND, ARTHUR H., M.D., Clinical Professor of Laryngology in the Medico-Chirurgical College; Laryngologist to the Medico-Chirurgical and the Presbyterian Hospitals; Laryngologist and Otologist to the Pennsylvania Institution for the Deaf and Dumb.
- \*1842. CLYMER, MEREDITH, M.D., New York.



## ELECTED

1871. COHEN, J. SOLIS, M.D., Professor (Honorary) of Laryngology in the Jefferson Medical College; Professor (Emeritus) of Diseases of the Throat in the Philadelphia Polyclinic; Consulting Physician to the Protestant Episcopal Mission; Physician to the Hospital for Diseases of the Lungs, Chestnut Hill.
1888. COHEN, SOLOMON SOLIS, M.D., Professor of Medicine and Therapeutics in the Philadelphia Polyclinic; Lecturer on Clinical Medicine in the Jefferson Medical College; Physician to the Philadelphia, the Rush and the Polyclinic Hospitals; Consulting Physician to the Jewish Hospital.
1898. COLES, STRICKER, M.D., Demonstrator of Obstetrics in the Jefferson Medical College; Assistant Obstetrician to the Jefferson Maternity.
1901. COLEY, THOMAS LUTHER, M.D., Assistant Physician to the Methodist Episcopal Hospital; Associate Editor of the *Therapeutic Monthly*; Assistant Editor of the *Philadelphia Medical Journal*.
1895. CROSS, WILLIAM A., M.D., Consulting Physician to the Jewish Hospital.
1884. CURTIN, ROLAND GIDEON, A.M., M.D., Ph.D., Physician to the Philadelphia and the Presbyterian Hospitals; Consulting Physician to St. Timothy's Hospital and the Rush Hospital for Consumptives.
1884. DA COSTA, JOHN C., M.D., Gynecologist to the Jefferson Medical College Hospital; Consulting Gynecologist to St. Agnes's Hospital; President of the Philadelphia Obstetrical Society.
1896. DA COSTA, JOHN CHALMERS, M.D., Professor of the Principles of Surgery and of Clinical Surgery in the Jefferson Medical College; Surgeon to Philadelphia and St. Joseph's Hospitals.
1887. DALAND, JUDSON, M.D., Instructor in Clinical Medicine in the University of Pennsylvania; Assistant Physician to the Hospital of the University of Pennsylvania; Professor of Clinical Medicine in the Philadelphia Polyclinic; Consulting Physician to the Kensington Hospital for Women.
1859. DARRACH, JAMES, M.D., Consulting Surgeon to the German-town Hospital.
1896. DAVIS, CHARLES N., M.D., Assistant Physician to the Dispensary for Diseases of the Skin in the Hospital of the

## ELECTED

University of Pennsylvania: Consulting Dermatologist to St. Mary's Hospital; Associate Physician in the Dispensary for Skin Diseases in the Howard Hospital; Associate Physician for Skin Diseases in the Northern Dispensary.

1888. DAVIS, EDWARD P., A.M., M.D., Professor of Obstetrics in the Jefferson Medical College and in the Philadelphia Polyclinic; Visiting Obstetrician to the Jefferson and Polyclinic Hospitals; Obstetrician and Gynecologist to the Philadelphia Hospital; Member of the American Gynecological Society, the American Pediatric Society and of the International Congress of Obstetrics and Gynecology.

1889. DAVIS, GWILYM G., M.D., (Univ. of Penna. and Goettingen), M.R.C.S. Eng., Assistant Professor of Applied Anatomy in the University of Pennsylvania; Surgeon to the Episcopal, St. Joseph's and Orthopædic Hospitals.

1900. DAVISSON, ALEX. HERON, M.D.

1894. DEAVER, HARRY C., M.D., Surgeon to the Episcopal, St. Mary's and Samaritan Hospitals and to St. Christopher's Hospital for Children.

1887. DEAVER, JOHN B., M.D., Surgeon-in-Chief to the German Hospital; Consulting Surgeon to the Germantown Hospital.

1892. DEAVER, RICHARD WILMOT, M.D.

1885. DERGUM, FRANCIS X., M.D., Clinical Professor of Neurology in the Jefferson Medical College; Neurologist to the Philadelphia Hospital; Consulting Neurologist to St. Agnes's and the Jewish Hospitals, and to the State Asylum for the Chronic Insane of Pennsylvania.

1891. DIXON, SAMUEL G., M.D., President and Executive Curator of the Academy of Natural Sciences of Philadelphia; Member of the Council of the American Philosophical Society; Member of the Board of Trustees of the Wistar Institute of Anatomy; Member of the Board of Managers of the Philadelphia Zoölogical Society.

1891. DIXON, WILLIAM C., M.D., Physician to the Industrial Home for Blind Women; Physician to the Shelter for Colored Orphans; Member of Consulting Staff of the Philadelphia Home for Incurables; Examiner of Insane Patients to the Philadelphia Hospital.

## ELECTED

1896. DONNELLAN, P. S., M.D., L.R.C.S. and P., Ireland; Laryngologist to St. Agnes's Hospital; Medical Examiner of the Mutual Life Insurance Company of New York.
1897. DORLAND, W. A. NEWMAN, M.D., Associate in Gynecology in the Philadelphia Polyclinic and College for Graduates in Medicine; Assistant Demonstrator of Obstetrics in the University of Pennsylvania.
1893. DOWNS, NORTON, M.D.
1864. DOWNS, R. N., M.D.
1884. DRYSDALE, T. M., M.D.
1864. DUER, EDWARD L., A.M., M.D., Gynecologist to the Presbyterian Hospital; Consulting Obstetrician to the Maternity Hospital and to the Preston Retreat.
1897. DUER, S. NAUDAIN, M.D., Physician to the Dispensary of the Presbyterian Hospital.
1871. DUHRING, L. A., M.D. Professor of Skin Diseases in the University of Pennsylvania.
1881. DULLES, CHARLES WINSLOW, M.D., Lecturer on the History of Medicine in the University of Pennsylvania; Surgeon to the Rush Hospital.
- \*1871. DUNGLISON, THOMAS R., M.D., Rosny sous Bois (Seine), France.
1860. DUNTON, WILLIAM R., M.D., Consulting Physician to the Germantown Hospital.
1899. EDSALL, DAVID L., M.D., Instructor in Clinical Medicine in the University of Pennsylvania; Assistant Physician to the University Hospital; Associate of the Pepper Laboratory of Clinical Medicine; Physician to the Home for Incurables and to St. Christopher's Hospital for Children; Pathologist to the Methodist Hospital.
- \*1887. EDWARDS, WILLIAM A., M.D., Physician to the Coronado Hospital, Coronado, California.
1896. ELY, THOMAS C., A.M., M.D.
1901. ERCK, THEODORE A., M.D., Assistant Surgeon to the Gynceean Hospital; Instructor in Gynecology in the Philadelphia Polyclinic and College for Graduates in Medicine; Gynecologist to the Frederick Douglass Memorial Hospital.
1893. ESHNER, AUGUSTUS A., M.D., Professor of Clinical Medicine in the Philadelphia Polyclinic and College for Graduates in

## FELLOWS

- Medicine; Physician to the Philadelphia Hospital; Assistant Physician to the Orthopaedic Hospital and Infirmary for Nervous Diseases; Physician to the Hospital for Diseases of the Lungs, at Chestnut Hill.
1880. ESKRIDGE, J. T., M.D., Neurologist to St. Luke's Hospital, and Consulting Alienist and Neurologist to the Arapahoe County Hospital, Denver, Colorado.
1868. EVANS, HORACE Y., A.M., M.D.
1894. FARIES, RANDOLPH, M.D., Surgeon to the Orthopedic Dispensary of the Hospital of the University of Pennsylvania; Director of Physical Education in the Protestant Episcopal Academy.
1893. FARR, WILLIAM W., M.D.
1884. FENTON, THOMAS H., M.D., Medical Director and Senior Ophthalmologist to the Union Mission Hospital; Ophthalmologist to St. Vincent's Home, to the Home for Aged Couples, to the Baptist Home and to the House of the Good Shepherd.
1884. FISHER, HENRY M., M.D., Physician to the Episcopal Hospital; Physician to the Out-patient Department of the Pennsylvania Hospital.
1900. FLEXNER, SIMON, M.D., Professor of Pathology in the University of Pennsylvania; Pathologist to the Philadelphia Hospital; Member of the Association of American Physicians; Corresponding Member of La Societa Medico-Chirurgica di Bologna.
1888. FLICK, LAWRENCE F., M.D.
1862. FORBES, WILLIAM S., M.D., Professor of Anatomy in the Jefferson Medical College; Clinical Surgeon to the Jefferson Medical College Hospital.
- †1885. FOX, JOSEPH M., M.D., Leesburg, Va.
1897. FRAZIER, CHARLES H., M.D., Professor of Clinical Surgery in the University of Pennsylvania; Surgeon to the University, Philadelphia and Howard Hospitals; Surgeon to the Home for Crippled Children.
- †1890. FREEMAN, WALTER J., M.D., Professor of Laryngology in the Philadelphia Polyclinic; Laryngologist to the Children's and Orthopaedic Hospitals; Consulting Laryngologist to the Pennsylvania Institution for the Deaf and Dumb.

## ELECTED

1900. FRENCH, MORRIS S., M.D.
1893. FRIEBIS, GEORGE, M.D., Ophthalmic Surgeon to the Lutheran Home and Orphanage, Mt. Airy.
1899. FURNESS, WILLIAM H., 3d, M.D.
1889. FUSSELL, M. HOWARD, M.D., Chief Physician to the Medical Dispensary of the Hospital of the University of Pennsylvania; Instructor in Clinical Medicine in the University of Pennsylvania.
1899. GAMELE, ROBERT G., M.D., One of the Attending Physicians to the Bryn Mawr Hospital.
1873. GERHARD, GEORGE S., M.D.
1864. GETCHELL, F. H., M.D.
1892. GIBB, JOSEPH S., M.D., Professor of Diseases of the Throat and Nose in the Philadelphia Polyclinic; Surgeon to the Ear, Nose, and Throat Department of the Episcopal Hospital.
1899. GIBBON, JOHN H., M.D., Surgeon to the Bryn Mawr Hospital; Assistant Surgeon to the Jefferson Medical College Hospital; Surgeon to the Out-patient Departments of the Pennsylvania and the Children's Hospitals.
1897. GIRVIN, JOHN H., M.D., Physician for Diseases of Women at the Presbyterian Hospital; Assistant Demonstrator of Obstetrics in the University of Pennsylvania.
1889. GITHENS, WILLIAM H. H., M.D., Visiting Physician to the Sheltering Arms.
1894. GLEASON, E. B., M.D., Clinical Professor of Otology in the Medico-Chirurgical College; Surgeon-in-Charge of the Nose, Throat, and Ear Department of the Northern Dispensary.
- \*1893. GOBRECHT, WILLIAM H., M.D., Washington, D. C.
1884. GODEY, HARRY, M.D.
1893. GOODELL, W. CONSTANTINE, M.D.
- †1897. GOULD, GEORGE M., A.M., M.D.
1894. GRAHAM, EDWIN E., M.D., Clinical Professor of Diseases of Children in the Jefferson Medical College; Physician to the Franklin Reformatory Home.
1885. GRAHAM, JOHN, M.D.
1891. GREEN, WALTER D., A.M., M.D.

## ELECTED

1883. GRIFFITH, J. P. CROZER, M.D., Clinical Professor of the Diseases of Children in the University of Pennsylvania; Physician to St. Agnes's, the Children's and the Methodist Hospitals.
- \*1889. GUITÉRAS, JOHN, M.D.
- \*1893. HAMILL, ROBERT H., M.D., Summit, N. J.
1894. HAMILL, SAMUEL McC., M.D., Professor of Diseases of Children in the Philadelphia Polyclinic and College for Graduates in Medicine; Instructor in Clinical Medicine in the University of Pennsylvania; Physician to the Medical Dispensary of the Hospital of the University of Pennsylvania; Physician to St. Christopher's Hospital for Children; Pediatricist to the Howard Hospital.
1897. HAND, ALFRED, JR., M.D., Dispensary Physician and Pathologist to the Children's Hospital; Pathologist and Bacteriologist to the Bryn Mawr Hospital; Dispensary Physician to the Methodist Hospital.
1886. HANSEL, HOWARD F., M.D., Clinical Professor of Ophthalmology in the Jefferson Medical College; Professor of Diseases of the Eye in the Philadelphia Polyclinic; Consulting Ophthalmologist to the Chester County Hospital and to the Frederick Douglass Memorial Hospital.
1889. HARE, HOBART A., M.D., Professor of Therapeutics in the Jefferson Medical College; Physician to the Jefferson Medical College Hospital.
1865. HARLAN, GEORGE C., M.D., Consulting Surgeon to the Wills Eye Hospital; Ophthalmic Surgeon to the Pennsylvania Hospital, and to the Pennsylvania Institution for the Blind; Emeritus Professor of Diseases of the Eye in the Philadelphia Polyclinic.
1885. HARTE, RICHARD H., M.D., Surgeon to the Pennsylvania and Episcopal Hospitals; Consulting Surgeon to St. Mary's and St. Timothy's Hospitals.
1888. HARTZELL, MILTON B., M.D., Instructor in Dermatology in the University of Pennsylvania; Dermatologist to the Methodist Episcopal Hospital.
1872. HAYS, I. MINIS, M.D.
1882. HEARN, W. JOSEPH, M.D., Clinical Professor of Surgery in the Jefferson Medical College; Surgeon to Philadelphia Hospital.



## ELECTED

1901. HEISLER, JOHN C., M.D., Professor of Anatomy in the Medico-Chirurgical College.
1884. HENRY, FREDERICK P., M.D., Physician to the Philadelphia Hospital; Professor of the Principles and Practice of Medicine in the Woman's Medical College of Pennsylvania.
1891. HEWSON, ADDINELL, A.M., M.D., Demonstrator of Anatomy in the Jefferson Medical College; Professor of Anatomy in the Philadelphia Polyclinic and College for Graduates in Medicine; Surgeon to St. Timothy's Hospital, Roxborough; Senior Surgeon to the Dispensary of the Episcopal Hospital.
1872. HINCKLE, A. G. B., M.D.
1897. HINCKLE, WILLIAM M., M.D., Lecturer on the Anatomy and Physiology of the Vocal Organs in the National School of Elocution and Oratory.
1892. HINSDALE, GUY, M.D., Consulting Physician to the Presbyterian Orphanage; Assistant Physician to the Orthopaedic Hospital and Infirmary for Nervous Diseases and to the Presbyterian Hospital.
1888. HIRSH, A. BERN., M.D., Physician to the Home for Aged Couples.
1888. HIRST, BARTON COOKE, M.D., Professor of Obstetrics in the University of Pennsylvania; Gynecologist to the Philadelphia and Howard Hospitals.
1894. HOCH, WILLIAM R., M.D., Instructor in Laryngology in the University of Pennsylvania; Laryngologist to the Methodist Episcopal Hospital.
1885. HOLLAND, JAMES W., M.D., Professor of Medical Chemistry and Toxicology in the Jefferson Medical College.
- †1879. HOPKINS, WILLIAM BARTON, M.D., Surgeon to the Pennsylvania Hospital.
1888. HORWITZ, ORVILLE, M.D., Professor of Genito-Urinary Diseases in the Jefferson Medical College; Surgeon to the Philadelphia Hospital and to the State Hospital for the Insane; Consulting Surgeon to the Hayes Mechanics' Home.
1868. HOWELL, SAMUEL B., M.D., Professor of Chemistry in the Medico-Chirurgical College.
1892. HUGHES, WILLIAM E., M.D., Professor of Clinical Medicine in the Medico-Chirurgical College; Visiting Physician to the

## ELECTED

- Philadelphia and Medico-Chirurgical Hospitals; Pathologist to the Presbyterian Hospital.
1898. HUTCHINSON, JAMES P., M.D., Surgeon to the Dispensaries of the Episcopal, Methodist, and Children's Hospitals.
1871. INGHAM, JAMES V., M.D.
- \*1885. JACKSON, EDWARD, M.D., Denver, Colorado, Emeritus Professor of Diseases of the Eye in the Philadelphia Polyclinic.
1887. JAYNE, HORACE, M.D., Ph.D., Professor of Zoology in the University of Pennsylvania; Director of the Wistar Institute of Anatomy and Biology.
1898. JOHNSON, RUSSELL H., A.B. (Princeton), M.D., Physician to the Pennsylvania Institution for the Deaf and Dumb.
1900. JONES, CHARLES JAMES, A.M., M.D.
1899. JOPSON, JOHN H., M.D., Surgeon to the Dispensaries of the Episcopal, Presbyterian and Children's Hospitals; Visiting Physician to the Philadelphia Home for Incurables.
1885. JUDD, LEONARDO DA VINCI, M.D.
1900. JUDSON, CHARLES F., A.B., M.D., Physician to the Episcopal Hospital; Physician to the Out-patient Departments of the Children's, the German and St. Christopher's Hospitals.
1886. JURIST, LOUIS, M.D.
- †1867. KEEN, WILLIAM W., M.D., LL.D., F.R.C.S. (Hon.), Professor of the Principles of Surgery and of Clinical Surgery in the Jefferson Medical College; Surgeon to the Jefferson Medical College Hospital; Membre Correspondant Étranger de la Société de Chirurgie de Paris; Membre Honoraire de la Société Belge de Chirurgie.
1897. KELLY, ALOYSIUS O. J., M.D., Instructor in Clinical Medicine in the University of Pennsylvania; Assistant Physician to the University Hospital; Clinical Professor of Pathology in the Woman's Medical College of Pennsylvania; Visiting Physician to St. Mary's and St. Agnes's Hospitals; Pathologist to the German Hospital.
- \*1887. KELLY, HOWARD A., M.D., Professor of Gynecology in Johns Hopkins University and Gynecologist to the Johns Hopkins Hospital, Baltimore, Md.

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1898. **KEMPTON, AUGUSTUS F., M.D.**
1895. **KNEASS, SAMUEL S., M.D.**, Associate in the William Pepper Laboratory of Clinical Medicine in the University of Pennsylvania.
1900. **KRUSEN, WILMER, M.D.**, Instructor in Gynecology in the Jefferson Medical College; Assistant Gynecologist and Chief of the Gynecological Dispensary of St. Joseph's Hospital; Consulting Gynecologist to the Children's Hospital in Germantown.
1897. **KYLE, D. BRADEN, M.D.**, Clinical Professor of Laryngology, Rhinology and Otology in the Jefferson Medical College; Consulting Laryngologist, Rhinologist and Otologist to St. Agnes's Hospital and to the Philadelphia Home for Incurables; Laryngologist to the New Jersey Training School for Feeble-minded Children; Bacteriologist to the Orthopaedic Hospital and Infirmary for Nervous Diseases.
- \*1892. **LAINÉ, DAMASO T., M.D.**, Havana, Cuba.
1865. **LA ROCHE, C. PERCY, M.D.**
1887. **LEAMAN, HENRY, M.D.**
1893. **LE CONTE, ROBERT G., M.D.**, Surgeon to the Pennsylvania, the Children's and the Bryn Mawr Hospitals.
1883. **LEFFMANN, HENRY, A.M., M.D., D.D.S.**, Professor of Chemistry and Toxicology in the Woman's Medical College of Pennsylvania; Professor of Chemistry in the Wagner Free Institute of Science; Member of the Society of Public Analysts.
1892. **LEIDY, JOSEPH, M.D.**, Physician to the Out-patient Department of the Pennsylvania Hospital; Consulting Physician to the Pennsylvania Training School for Feeble-minded Children.
1855. **LEWIS, FRANCIS W., M.D.**
1877. **LEWIS, MORRIS J., M.D.**, Physician to the Children's Hospital, to the Orthopaedic Hospital and Infirmary for Nervous Diseases and to the Pennsylvania Hospital.
1886. **LLOYD, J. HENDRIE, M.D.**, Physician to the Methodist Episcopal Hospital and to the Home for Crippled Children; Consulting Neurologist to the State Asylum for the Chronic Insane of Pennsylvania and to the Pennsylvania Training School for Feeble-minded Children.

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1900. LODGE, JOHN W., M.D., Consulting Physician to the Bryn Mawr Hospital.
1893. LONGAKER, DANIEL, M.D.
1877. LONGSTRECH, MORRIS, M.D.
1900. MCCABBY, DANIEL J., M.D., Instructor in Neurology in the Philadelphia Polyclinic; Associate of the William Pepper Laboratory of Clinical Medicine.
1875. MCCLELLAN, GEORGE, M.D., Consulting Surgeon to the Howard Hospital.
1895. MCFARLAND, JOSEPH, M.D., Professor of Pathology and Bacteriology in the Medico-Chirurgical College; Pathologist to the Medico-Chirurgical and the Philadelphia Hospitals.
1900. McREYNOLDS, ROBERT PHILLIPS, M.D., One of the Resident Chiefs and one of the Chiefs of the Gynecological Dispensary of the Presbyterian Hospital.
1886. MACCOY, ALEXANDER W., M.D., Surgeon for Diseases of the Nose and Throat in the Out-patient Department of the Pennsylvania Hospital; Member of the American Laryngological Society.
1901. MACLEOD, GEORGE I., JR., M.D., Registrar of the Bryn Mawr Hospital.
1896. MAKUEN, G. HUDSON, M.D., Professor of Defects of Speech in the Philadelphia Polyclinic; Laryngologist to St. Mary's Hospital and to the Frederick Douglass Memorial Hospital; Visiting Consultant on Defects of Speech to the New Jersey Training School for Feeble-minded Children.
- \*1885. MALLEY, JOHN WILLIAM, M.D., Ph.D. (Goett.), LL.D. (Princeton), F.R.S., Professor of Chemistry in the University of Virginia.
1898. MARSHALL, GEORGE MORLEY, M.D., Laryngologist to the Philadelphia Hospital; Physician and Laryngologist to St. Joseph's Hospital.
1893. MARSHALL, JOHN, M.D., Professor of Chemistry and Toxicology in the University of Pennsylvania.
1889. MARTIN, EDWARD, M.D., Professor of Clinical Surgery in the University of Pennsylvania; Surgeon to the University, Howard, St. Agnes's, Philadelphia and Bryn Mawr Hospitals.

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1885. MAYS, THOMAS J., M.D., Visiting Physician to the Rush Hospital.
- \*1868. MEARS, J. EWING, M.D.
1875. MERG, ARTHUR V., M.D., Physician to the Pennsylvania Hospital; Consulting Physician to the Pennsylvania Institution for the Instruction of the Blind.
- \*1884. MIFFLIN, HOUSTON, M.D., Columbia, Pa.
1894. MILLER, D. J. MILTON, M.D., Physician to the Episcopal Hospital; Assistant Physician to the Children's Hospital.
1881. MILLS, CHARLES K., M.D., Clinical Professor of Nervous Diseases in the University of Pennsylvania; Neurologist to the Philadelphia Hospital.
- †1888. MITCHELL, JOHN K., M.D., Assistant Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases; Assistant Neurologist to the Presbyterian Hospital; Attending Physician to the Pennsylvania Training School for Feeble-minded Children.
1856. MITCHELL, S. WEIR, M.D., M. Nat. Ac. Sci., LL.D. (Harvard, Edinburgh and Princeton); M.D. *Honoris Causa* (Bologna, Italy); Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases; Physician to the Presbyterian Hospital.
1882. MONTGOMERY, EDWARD E., M.D., Professor of Gynecology in the Jefferson Medical College; Gynecologist to the Jefferson and St. Joseph's Hospitals.
1863. MOREHOUSE, GEORGE READ, M.D., Ph.D. (Princeton), Consulting Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases.
1886. MORRIS, CASPAR, M.D.
1893. MORRIS, ELLISTON J., M.D., Physician to the Episcopal Hospital, the Sheltering Arms and the Midnight Mission.
1883. MORRIS, HENRY, M.D., Visiting Physician to St. Joseph's Hospital.
1856. MORRIS, J. CHESTON, M.D.
1897. MORTON, SAMUEL W., M.D.
1861. MORTON, THOMAS G., M.D., Senior Surgeon and President of the Medical Staff of the Pennsylvania Hospital; Fellow of the American Surgical Association.
1891. MORTON, THOMAS S. K., M.D., Professor of Surgery in the Philadelphia Polyclinic and College for Graduates in Medi-

## ELECTED

cine; Surgeon to the Out-patient Department of the Pennsylvania Hospital; Consulting Surgeon to the Woman's Hospital and the Philadelphia Dispensary.

1864. MOSS, WILLIAM, M.D.

1890. MÜLLER, AUGUSTE F., M.D., Attending Physician to the Germantown Hospital.

1882. MUSSER, JOHN H., M.D., Professor of Clinical Medicine in the University of Pennsylvania; Physician to the University, the Philadelphia and the Presbyterian Hospitals.

1896. MYERS, T. D., M.D.

1886. NEFF, JOSEPH S., M.D.

1887. NEILSON, THOMAS RUNDLE, M.D., Surgeon to the Episcopal Hospital and to St. Christopher's Hospital for Children; Professor of Genito-Urinary Surgery in the Philadelphia Polyclinic; Clinical Assistant Professor of Genito-Urinary Diseases in the University of Pennsylvania.

1899. NICHOLSON, WILLIAM R., JR., M.D., Instructor in Gynecology and Assistant Demonstrator of Obstetrics in the University of Pennsylvania; Obstetrician to the Maternity Hospital; Assistant Surgeon to the Gynceean Hospital.

1889. NOBLE, CHARLES P., M.D., Surgeon-in-Chief to the Kensington Hospital for Women; Surgeon-in-Charge of the Department for Women of the Northern Dispensary and of the Union Mission Hospital; Clinical Professor of Gynecology in the Woman's Medical College of Pennsylvania; Lecturer on Gynecology in the Philadelphia Polyclinic.

1893. NOBLE, WILLIAM H., M.D.

1898. NOLAN, EDWARD J., M.D., Recording Secretary and Librarian of the Academy of Natural Sciences of Philadelphia.

1901. NORRIS, HENRY, M.D., Chief of the Surgical Dispensary of the Hospital of the University of Pennsylvania; Clinical Assistant in the Clinic for Genito-Urinary Surgery in the Polyclinic Hospital.

1869. NORRIS, HERBERT, M.D.

1865. NORRIS, ISAAC, M.D.

1892. NORRIS, RICHARD C., M.D., Lecturer on Clinical and Operative Obstetrics in the University of Pennsylvania; Obstetrician in Charge to the Preston Retreat; Visiting Obstetrician



## ELECTED

to the Philadelphia Hospital; Gynecologist to the Methodist Hospital and Consulting Obstetrician and Attending Gynecologist to the Southeastern Dispensary and Hospital.

1884. OLIVER, CHARLES A., A.M., M.D., Surgeon to Wills Eye Hospital; Ophthalmic Surgeon to the Philadelphia and the Presbyterian Hospitals; Consulting Ophthalmic Surgeon to St. Timothy's Hospital.
1884. O'NEILL, J. WILKS, M.D.
- \*1885. OSLER, WILLIAM, M.D., Professor of Medicine in Johns Hopkins University and Physician to the Johns Hopkins Hospital, Baltimore, Md.
1897. PACKARD, FRANCIS R., M.D., Dean of the Philadelphia Polyclinic and College for Graduates in Medicine; Surgeon for Diseases of the Ear in the Out-patient Department of the Pennsylvania Hospital; Instructor in Laryngology in the University of Pennsylvania.
1890. PACKARD, FREDERICK A., M.D., Visiting Physician to the Pennsylvania and Children's Hospitals.
1858. PACKARD, JOHN H., M.D., Late Surgeon to the Pennsylvania Hospital; Surgeon Emeritus to St. Joseph's Hospital.
1898. PAGE, HENRY F., M.D., Assistant Physician to the German Hospital and Physician to the Medical Dispensary of the same; Instructor in Clinical Medicine in the Woman's Medical College of Pennsylvania; Physician to the Baptist Home.
1882. PARISH, WILLIAM H., M.D., Professor of Obstetrics in the Dartmouth Medical College; Professor of Anatomy in the Woman's Medical College of Pennsylvania; Consulting Obstetrician to the Lying-in Charity Hospital; Consulting Surgeon to the Kensington Hospital; Medical Director and Gynecologist to St. Agnes's Hospital.
1899. PARKE, WILLIAM E., M.D., Assistant Surgeon in the Department for Diseases of Women of the Northern Dispensary; Clinical Assistant and Surgeon to the Dispensary of the Kensington Hospital for Women.
1898. PEARCE, F. SAVARY, M.D., Clinical Professor of Nervous and Mental Diseases in the Medico-Chirurgical College of Phila-

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delphia; Neurologist to the Philadelphia and Howard Hospitals; Secretary of the Section on Nervous and Mental Diseases of the American Medical Association.

†1889. PENROSE, CHARLES BINGHAM, M.D.

1854. PENROSE, R. A. F., M.D., LL.D., Professor (Emeritus) of Obstetrics and Diseases of Women and Children in the University of Pennsylvania.

1884. PERKINS, FRANCIS M., M.D., Ophthalmic Surgeon to St. Agnes's Hospital.

1899. PHILLIPS, JOHN L., M.D.

1883. PIERSOL, GEORGE A., M.D., Professor of Anatomy in the University of Pennsylvania.

1872. PORTER, WILLIAM G., M.D., Surgeon to the Presbyterian Hospital; Consulting Physician to the Philadelphia Dispensary and to the Educational Home for Boys.

1896. POSEY, WM. CAMPBELL, M.D., Professor of Ophthalmology in the Philadelphia Polyclinic and College for Graduates in Medicine; Ophthalmologist to the Howard and Epileptic Hospitals; Assistant Surgeon to Wills Eye Hospital.

1885. POTTER, THOMAS C., M.D.

1899. POTTS, CHARLES S., M.D., Instructor in Nervous Diseases in the University of Pennsylvania; Neurologist to the Philadelphia Hospital; Consulting Physician to the Hospital for the Insane of Atlantic County, New Jersey; Consulting Physician to the Penitentiary, Eastern District of Pennsylvania.

†1899. PRICE, JOSEPH, M.D., Obstetric Physician to the Philadelphia Dispensary.

1887. RANDALL, B. ALEXANDER, M.A., M.D., Clinical Professor of Diseases of the Ear in the University of Pennsylvania; Professor of Diseases of the Ear in the Philadelphia Polyclinic; Eye and Ear Surgeon to the Children's Hospital; Consulting Aurist to the Pennsylvania Institution for the Deaf and Dumb.

1887. REED, CHARLES H., M.D.

1885. REICHERT, EDWARD T., M.D., Professor of Physiology in the University of Pennsylvania.

1897. RHEIN, JOHN H. W., M.D., Neurologist to St. Agnes's Hospital; Assistant Physician to the Orthopaedic Hospital and Infirm-

## ELECTED

- ary for Nervous Diseases; Physician to the Philadelphia Home for Incurables; Bacteriologist to the Pennsylvania Training School for Feeble-minded Children.
1891. RHOADS, EDWARD G., M.D.
1898. RIESMAN, DAVID, M.D., Professor of Clinical Medicine in the Philadelphia Polyclinic; Instructor in Clinical Medicine in the University of Pennsylvania; Physician to the Philadelphia Hospital; Neurologist to the Northern Dispensary.
1895. RING, G. ORAM, M.D., Ophthalmic Surgeon to the Episcopal Hospital; Ophthalmic and Aural Surgeon to the Samaritan Hospital.
1891. RISLEY, S. D., M.D., Attending Surgeon to the Wills Eye Hospital; Professor (Emeritus) of Ophthalmology in the Philadelphia Polyclinic and College for Graduates in Medicine; Member of the Board of Managers of the Pennsylvania Training School for Feeble-minded Children; Alumnus Manager of the University Hospital.
- †1878. ROBERTS, JOHN B., M.D., Professor of Anatomy and Surgery in the Philadelphia Polyclinic; Surgeon to the Methodist Hospital.
1899. ROBERTS, WALTER, M.D., Instructor in Otology in the Philadelphia Polyclinic; Physician to the Ear, Nose and Throat Department of the Dispensary of St. Christopher's Hospital for Children; Clinical Assistant for Diseases of the Nose and Throat in the Out-patient Department of the Pennsylvania Hospital.
- \*1888. ROBINS, ROBERT P., M.D.
1900. RODMAN, WILLIAM L., M.D., Professor of the Principles of Surgery and Clinical Surgery in the Medico-Chirurgical College; Professor of the Principles and Practice of Surgery in the Woman's Medical College of Pennsylvania.
1898. ROSS, GEORGE G., M.D., Assistant Surgeon to the German Hospital and Surgeon to the Out-patient Department of the same.
1897. SAILER, JOSEPH, M.D., Associate in the Pepper Clinical Laboratory in the University of Pennsylvania; Pathologist to the Pennsylvania Training School for Feeble-minded Children.
1900. SAJOUS, CHARLES E. DE M., M.D.

## ELECTED

†1866. SCHÄFFER, CHARLES, M.D.

1899. SCHANBERG, JAY F., M.D., Professor of Diseases of the Skin in the Philadelphia Polyclinic and College for Graduates in Medicine; Assistant Attending Physician to the Municipal Hospital of Philadelphia.

1887. DE SCHWEINITZ, GEORGE E., M.D., Professor of Ophthalmology in the Jefferson Medical College; Ophthalmic Surgeon to the Philadelphia Hospital; Ophthalmologist to the Orthopedic Hospital and Infirmary for Nervous Diseases; Consulting Ophthalmologist to the Philadelphia Polyclinic and College for Graduates in Medicine, to the Bryn Mawr Hospital and to the Chester County Hospital.

1895. SCOTT, J. ALISON, M.D., Instructor in Clinical Medicine in the University of Pennsylvania; Visiting Physician to the Pennsylvania Hospital; Physician to the Church Home for Children.

1892. SEISS, RALPH W., M.D., Professor of Otology in the Philadelphia Polyclinic; Consulting Laryngologist to the Pennsylvania Institution for the Deaf and Dumb.

1888. SELTZER, CHARLES M., M.D.

1884. SHAFFNER, CHARLES, M.D.

1897. SHARPLESS, W. T., M.D., Physician to the Chester County Hospital, West Chester, Pa.

1876. SHIPPEN, EDWARD, A.M. (Princeton), M.D., Medical Director U. S. Navy (retired).

1891. SHOBER, JOHN B., A.M., M.D., Associate Gynecologist to the Gynceean Hospital; Gynecologist to the Howard Hospital; Obstetrician to the Philadelphia Hospital.

1890. SHOEMAKER, GEORGE ERETY, A.M., M.D., Gynecologist to the Presbyterian Hospital, and to the Pennsylvania Epileptic Hospital and Colony Farm.

†1893. SHOEMAKER, HARVEY, M.D., Visiting Physician to the Sheltering Arms and to the Southern Home for Destitute Children; Assistant Physician to the German Hospital; Physician to the Out-patient Departments of the German and Pennsylvania Hospitals.

†1896. SHOEMAKER, WILLIAM T., M.D., Assistant Ophthalmologist to the German Hospital and Ophthalmic Surgeon to the Out-patient Department of the same; Ophthalmic Surgeon

## ELECTED

to the Out-patient Department of the Presbyterian Hospital; Ophthalmologist to the Southern Home for Destitute Children.

1900. SHUMWAY, EDWARD ADAMS, B.S., M.D.

1880. SIMES, J. HENRY C., M.D., Emeritus Professor of Genito-Urinary and Venereal Diseases in the Philadelphia Polyclinic.

1872. SINKLER, WHARTON, M.D., Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases; Neurologist to the State Asylum for the Chronic Insane of Pennsylvania.

1895. SLOCUM, HARRIS A., M.D., Professor of Gynecology in the Philadelphia Polyclinic; Gynecologist to St. Clement's Hospital for Epileptics.

1895. SPELLISSY, JOSEPH M., A.M., M.D., Surgeon to St. Joseph's and the Methodist Episcopal Hospitals; Assistant Surgeon to Orthopedic Dispensary of University Hospital; Surgeon to the Out-patient Department of the Pennsylvania Hospital.

1897. SPILLER, WILLIAM G., M.D., Assistant Clinical Professor of Nervous Diseases in the University of Pennsylvania; Clinical Professor of Nervous Diseases in the Woman's Medical College of Pennsylvania; Professor of Nervous Diseases in the Philadelphia Polyclinic and College for Graduates in Medicine; Neurologist to the Philadelphia Hospital.

1894. STAHL, B. FRANKLIN, Ph.G., B.S., M.D., Instructor in Physical Diagnosis, and Lecturer on Dietetics of the Sick in the University of Pennsylvania; Visiting Physician to St. Agnes's Hospital; Neurological Registrar to Philadelphia Hospital.

1875. STARR, LOUIS, M.D.

1898. STEELE, J. DUTTON, M.D., Instructor in Medicine in the University of Pennsylvania; Physician to the Medical Dispensary of the University Hospital; Bacteriologist to the Presbyterian Hospital.

1892. STEINBACH, LEWIS W., M.D., Professor of Clinical and Operative Surgery in the Philadelphia Polyclinic; Visiting Surgeon to the Philadelphia and the Jewish Hospitals.

1884. STELWAGON, HENRY W., M.D., Ph.D., Clinical Professor of Dermatology in the Jefferson Medical College and in the Woman's Medical College; Physician to the Department for Skin Diseases of the Howard Hospital; Socio Corrispondente di la Societa Italiano di Dermatologia e Sifilografia.

## ELECTED

1895. STENGEL, ALFRED, M.D., Professor of Clinical Medicine in the University of Pennsylvania; Physician to the University, Pennsylvania, and Children's Hospitals.
1901. STEVENS, ARTHUR A., M.D., Professor of Pathology in the Woman's Medical College of Pennsylvania; Lecturer on Physical Diagnosis in the University of Pennsylvania; Physician to the Episcopal and to St. Agnes's Hospitals.
1888. STEWART, DAVID D., M.D., Professor in the Philadelphia Polyclinic; Attending Physician to the Episcopal Hospital; Consulting Physician to the Kensington Hospital for Women.
1898. STILES, GEORGE M., M.D.
1898. STOUT, GEORGE C., M.D., Laryngologist and Aurist to St. Mary's Hospital and to the Children's Aid Society; Associate in Otolary in the Philadelphia Polyclinic and College for Graduates in Medicine.
1884. STRYKER, SAMUEL S., M.D., Physician to the Presbyterian Hospital.
1900. SWAN, JOHN M., M.D., Demonstrator of Osteology and Assistant Demonstrator of Anatomy in the University of Pennsylvania; Dispensary Physician to the Presbyterian Hospital.
1898. SWEET, WILLIAM M., M.D., Associate in Ophthalmology in the Philadelphia Polyclinic; Instructor in Ophthalmology, and Chief Clinical Assistant in the Out-patient Eye Department of the Jefferson Medical College; Ophthalmic Surgeon to the Phoenixville Hospital.
1900. TALLEY, JAMES ELY, A.B., M.D., Physician to the Out-patient Department of the Presbyterian Hospital; Assistant and Consulting Physician to the Country Branch of the Children's Hospital.
1901. TAYLOR, J. GURNEY, M.D.
1886. TAYLOR, JOHN MADISON, M.D., Pediatricist to the Philadelphia Hospital; Assistant Physician to the Orthopaedic Hospital and Infirmary for Nervous Diseases; Assistant Physician to the Children's Hospital.
1887. TAYLOR, WILLIAM J., M.D., Surgeon to the Orthopaedic Hospital and Infirmary for Nervous Diseases, and to St. Agnes's Hospital; Consulting Surgeon to the West Philadelphia Hospital for Women.
1886. TAYLOR, WILLIAM L., M.D.

## ELECTED

1867. THOMAS, CHARLES HERMON, M.D.
1897. THOMSON, A. G., M.D., Ophthalmic Surgeon to the Children's Hospital; Assistant Surgeon to Wills Eye Hospital; Assistant Ophthalmologist to the Orthopaedic Hospital and Infirmary for Nervous Diseases.
- †1869. THOMSON, WILLIAM, M.D., Emeritus Professor of Ophthalmology in the Jefferson Medical College; Surgeon to Wills Eye Hospital.
1896. THORINGTON, JAMES, A.M., M.D., Professor of Diseases of the Eye in the Philadelphia Polyclinic.
1898. THORNTON, EDWARD Q., M.D., Demonstrator of Therapeutics in the Jefferson Medical College.
1896. TOULMIN, HARRY, M.D., Assistant Medical Director of the Penn Mutual Life Insurance Company.
1901. TUCKER, HENRY, M.D., Demonstrator of Genito-Urinary Diseases in the Jefferson Medical College; Assistant Surgeon to the Genito-Urinary Department of Jefferson Medical College Hospital.
- †1894. TUNIS, JOSEPH PRICE, M.D., Formerly Assistant Demonstrator of Anatomy and of Surgery in the University of Pennsylvania; Surgeon to the Methodist Hospital.
1901. TURNER, JOHN B., M.D., Clinical Assistant at the Wills Eye Hospital.
1866. TYSON, JAMES, A.M., M.D., Professor of Medicine in the University of Pennsylvania and Physician to the Hospital of the University of Pennsylvania; Physician to the Philadelphia Hospital; Member of the Association of American Physicians.
1897. TYSON, T. MELLOR, M.D., Assistant Physician to the Hospital of the University of Pennsylvania; Physician to the Rush Hospital, the Philadelphia Lying-in Charity Hospital and the Children's Aid Society of Philadelphia.
1864. VANDYKE, EDWARD, B., A.M., M.D.
1873. VAN HARLINGEN, ARTHUR, Ph.B. (Yale), M.D., Emeritus Professor of Dermatology in the Philadelphia Polyclinic; Dermatologist to the Children's Hospital.
1893. VANSANT, EUGENE LARUE, M.D., Professor of Diseases of the Throat and Nose in the Philadelphia Polyclinic; Visiting Physician to the Throat, Nose and Ear Department of the Howard Hospital.



## ELECTED

1897. VEASEY, CLARENCE A., M.D., Adjunct Professor of Diseases of the Eye in the Philadelphia Polyclinic and College for Graduates in Medicine; Demonstrator of Ophthalmology in the Jefferson Medical College; Chief Clinical Assistant to the Ophthalmological Department of the Jefferson Medical College Hospital; Consulting Ophthalmologist to the Philadelphia Lying-in Charity Hospital.
- †1883. VINTON, CHARLES HARROD, M.D.
1885. WALKER, JAMES B., M.D., Ph.D., Consulting Physician to the West Philadelphia Hospital for Women and Children.
1893. WARREN, JOSEPH W., M.D., Associate Professor of Physiology in Bryn Mawr College.
1895. WATSON, ARTHUR W., M.D., Professor of Diseases of the Throat and Nose in the Philadelphia Polyclinic; Laryngologist to the Howard Hospital and to the Hospital for Diseases of the Lungs, Chestnut Hill.
1886. WATSON, EDWARD W., M.D.
1875. WEBB, WILLIAM H., M.D.
1883. WELCH, WILLIAM M., M.D., Physician-in-Charge of the Municipal Hospital for Contagious Diseases; Consulting Physician to the Northern Dispensary and to the Northern Home for Friendless Children.
1897. WELLS, WILLIAM H., M.D., Adjunct Professor of Obstetrics and Diseases of Infancy in the Philadelphia Polyclinic; Demonstrator of Clinical Obstetrics in the Jefferson Medical College.
1893. WESTCOTT, THOMPSON S., M.D., Instructor in Diseases of Children in the University of Pennsylvania; Visiting Physician to the Methodist Episcopal Hospital; Assistant Physician to the Children's Hospital.
1884. WHARTON, HENRY R., M.D., Clinical Professor of Surgery in the Woman's Medical College of Pennsylvania; Surgeon to the Presbyterian and Children's Hospital; Consulting Surgeon to the Bryn Mawr Hospital, St. Christopher's Hospital for Children and the Pennsylvania Institution for the Deaf and Dumb.
1901. WHITE, COURTLAND Y., M.D., Assistant Director of the William Pepper Laboratory of Clinical Medicine; Instructor of Clinical



## ELECTED

Medicine in the University of Pennsylvania; Assistant Physician to the University Hospital; Demonstrator of Pathology in the Veterinary Department of the University of Pennsylvania.

1878. WHITE, J. WILLIAM, M.D., Ph.D., John Rhea Barton Professor of Surgery in the University of Pennsylvania; Surgeon to the University Hospital; Fellow of the American Surgical Association and of the American Association of Genito-Urinary Surgeons.
1898. WHITING, ALBERT D., M.D., Assistant Surgeon and Registrar to the German Hospital, and Surgeon to the Out-patient Department of the same; Physician to the Southern Home for Destitute Children.
- †1880. WILLARD, DE FOREST, A.M., M.D., Ph.D., Clinical Professor of Orthopedic Surgery in the University of Pennsylvania; Surgeon to the Presbyterian Hospital; President of the American Surgical Association; Chairman of the Surgical Section of the American Medical Association.
- \*1878. WILLIAMSON, JESSE, M.D., Wilmington, Delaware, one of the Surgeons to the Delaware Hospital.
1881. WILSON, H. AUGUSTUS, M.D., Emeritus Professor of Orthopedic Surgery in the Philadelphia Polyclinic; Clinical Professor of Orthopedic Surgery in the Jefferson Medical College; Consulting Orthopedic Surgeon to the Philadelphia Lying-in Charity Hospital and to the Kensington Hospital for Women.
1874. WILSON, JAMES C., M.D., Professor of the Practice of Medicine and of Clinical Medicine in the Jefferson Medical College, and Physician to the Hospital of the same (Faculty Staff); Physician-in-Chief to the German Hospital; Attending Physician to the Pennsylvania Hospital.
1897. WILSON, W. REYNOLDS, M.D., Visiting Physician to the Philadelphia Lying-in Charity Hospital.
- †1884. WIRGMAN, CHARLES, M.D., Physician to the Jefferson Medical College Hospital and to the Howard Hospital; Physician to the Out-patient Department of the Children's Hospital.
1901. WITMER, A. FERREE, M.D., Instructor in Nervous Diseases in the Philadelphia Polyclinic and College for Graduates in Medicine.

## FELLOWS

1893. WOOD, ALFRED C., M.D., Demonstrator of Surgery in the University of Pennsylvania; Assistant Surgeon to the University Hospital; Surgeon to the Philadelphia Hospital.
1900. WOOD, GEORGE B., M.D., Instructor in Laryngology in the University of Pennsylvania; Assistant in the Clinic for Diseases of the Nose and Throat at the Polyclinic Hospital.
1865. WOOD, HORATIO C., M.D., LL.D. (Yale and Lafayette); Professor of Materia Medica and Therapeutics in the University of Pennsylvania; Associate Fellow in Medicine and Surgery of the American Academy of Arts and Sciences; Member of the National Academy of Science.
1880. WOODBURY, FRANK, M.D., Associate in Laryngology in the Philadelphia Polyclinic.
1866. WOODS, D. F., M.D., Physician to the Presbyterian Hospital.
1901. WOODS, RICHARD F., M.D., Assistant Surgeon to the Gyneccean Hospital.
1888. WOODWARD, CHARLES E., M.D., Secretary of the West Chester Board of Health; U. S. Examining Surgeon; Member of the Medical Staff of the Chester County Hospital.
- †1897. WOODWARD, GEORGE, M.D.
1860. WURTS, CHARLES STEWART, M.D.
1868. YARROW, THOMAS J., M.D.
1889. YOUNG, JAMES K., M.D., Professor of Orthopedic Surgery in the Philadelphia Polyclinic; Clinical Professor of Orthopedic Surgery in the Woman's Medical College of Pennsylvania; Instructor in Orthopedic Surgery in the University of Pennsylvania and Assistant Orthopedic Surgeon to the University Hospital.
1894. ZENTMAYER, WILLIAM, M.D., Attending Surgeon to Wills Eye Hospital; Ophthalmic Surgeon to St. Mary's Hospital; Ophthalmologist to the House of Refuge.
1899. ZIEGLER, S. LEWIS, M.D., Ophthalmic Surgeon to St. Joseph's Hospital.
1887. ZIEGLER, WALTER M. L., A.M., M.D.
1895. ZIMMERMAN, MASON W., M.D., Ophthalmic Surgeon to the Germantown Hospital and to St. Christopher's Hospital for Children.

## ASSOCIATE FELLOWS.

[Limited to Fifty, of whom Twenty may be Foreigners.]

### AMERICAN.

#### ELECTED

- 1876. BILLINGS, JOHN S., M.D., U. S. A. (retired), New York.
- 1886. BOWDITCH, HENRY P., M.D., Boston, Massachusetts.
- 1877. CHAILLÉ, STANFORD E., M.D., New Orleans, Louisiana.
- 1886. CHEEVER, DAVID W., M.D., Boston, Massachusetts.
- 1896. CONNER, PHINEAS SANBORN, M.D., Cincinnati, Ohio.
- 1893. COUNCILMAN, WILLIAM T., M.D., Boston, Massachusetts.
- 1876. DAVIS, N. S., M.D., Chicago, Illinois.
- 1892. EMMET, THOMAS ADDIS, M.D., New York.
- 1892. FITZ, REGINALD H., M.D., Boston, Massachusetts.
- 1895. FLETCHER, ROBERT, M.D., Washington, D. C.
- 1891. JACOBI, A., M.D., New York.
- 1895. MCBURNEY, CHARLES, M.D., New York.
- 1876. MOORE, E. M., M.D., Rochester, New York.
- 1886. REEVE, JOHN C., M.D., LL.D., Dayton, Ohio.
- 1886. SENN, NICHOLAS, M.D., Chicago, Illinois.
- 1896. STERNBERG, GEORGE M., M.D., U. S. A., Washington, D. C.
- 1886. THOMAS, T. GAILLARD, M.D., New York.
- 1896. TIFFANY, L. McLANE, M.D., Baltimore, Maryland.
- 1894. WARREN, J. COLLINS, M.D., Boston, Massachusetts.
- 1894. WEIR, ROBERT F., M.D., New York.
- 1892. WELCH, WILLIAM H., M.D., Baltimore, Maryland.

### FOREIGN.

- 1890. BACCELLI, GUIDO, Rome, Italy.
- 1877. BARNES, ROBERT, M.D., London, England.
- 1894. BRUNTON, SIR T. LAUDER, M.D., London, England.

xxxiv ASSOCIATE AND CORRESPONDING MEMBERS.

ELECTED

1883. FAYRER, SIR JOSEPH, M.D., LL.D., F.R.S., London, England.  
1899. FRASER, THOMAS R., M.D., LL.D., F.R.C.P., F.R.S., Edinburgh, Scotland.  
1883. HEATH, CHRISTOPHER, F.R.C.S., London, England.  
1896. JACCOUD, PROF. S., M.D., Paris, France.  
1874. JACKSON, J. HUGHLINGS, M.D., London, England.  
1893. V. JAKSCH, RUDOLF, M.D., Prague, Bohemia.  
1896. LEYDEN, ERNST, M.D., Berlin, Germany.  
1877. LORD LISTER, M.D., LL.D., F.R.S., London, England.  
1873. OGLE, JOHN W., M.D., London, England.  
1898. RODDICK, THOMAS G., M.D., Montreal, Canada.  
1896. PYE-SMITH, P. H., M.D., London, England.  
1869. VALCOURT, TH. DE, M.D., Cannes, France.  
1892. VIRCHOW, RUDOLF, M.D., Berlin, Germany.

CORRESPONDING MEMBERS.

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ELECTED

1880. CARROW, FLEMMING, M.D., United States.  
1880. CHIARA, DOMENICO, M.D., Florence, Italy.  
1886. DEY, KANNY LALL, M.D., Calcutta, India.  
1885. RENDU, JEAN, M.D., Lyons, France.

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## NECROLOGICAL LIST.

### FELLOWS.

ANDREW K. SMITH (Non-resident),	August 14, 1899.
RICHARD J. DUNGLISON,	March 4, 1901.
CHARLES RAY KING (Non-resident),	April 5, 1901.
JOHN H. GROVE,	April 6, 1901.
SAMUEL ASHHURST,	November 12, 1901.
WILLIAM F. NORRIS,	November 18, 1901.

### ASSOCIATE FELLOWS.

HENRY W. ACLAND,	October 16, 1900.
WILLIAM H. DRAPER,	April 26, 1901.
JOHN G. KERR,	1901.
SIR WILLIAM MACCORMAC,	December 4, 1901.

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## MEMOIR OF SIR JAMES PAGET.<sup>1</sup>

By JOHN CHALMERS DA COSTA, M.D.

[Read February 6, 1901.]

DEATH is ever busy with his shuttle, and with tireless fingers weaves his sombre thread into all the warp and woof of the affairs of men. The story of Death is as old as mankind; its mystery is never fading, and we still cry, with Shelley, "How wonderful is Death—Death and his brother, Sleep!" He is still called the King of Terrors; yet with the advance of civilization has come the knowledge that death is an inevitable consequence and not a supernatural punishment. As Lecky puts it, "It is a remedy rather than a sentence;" and when a man full of years and honors comes to die we weep for his loss, we grieve that humanity is deprived of his services, but we rest in calm confidence that he lies down to "pleasant dreams."

A large soul has recently passed away; a beacon of science has been extinguished. The dark sceptre of the Destroyer was raised, and a mighty spirit fell at the command. The spectral fingers of Life's Night drew the curtain, and James Paget was gathered to the bosom of Infinity.

Sir James Paget was born in Yarmouth on January 11, 1814—Yarmouth, a town known to us all, not only because of its great fisheries, its shipyards, the famous historical characters and important events with which it has been connected, but also because it is linked with the names of Steerforth and Peggotty, Mr. Barkis and David Copperfield. Paget was born in the dawn of the cen-

<sup>1</sup> Incidents in the life of Paget were taken from obituary notices in the *Lancet*, *British Medical Journal*, and the *Practitioner*.

ury, and was destined to witness practically all of the wonderful changes of the nineteenth century—all the marvels of the busy Age of Steam. The time of his birth was the age of Rogers and Moore, Byron and Campbell, Richard Brinsley Sheridan and Beau Brummel. England was ruled by George, the Prince Regent. Napoleon, at the head of three hundred thousand men, was striving with gigantic effort to drive the Allies out of France, and both the Allies and the soldiers of the Empire were armed with the flint-lock musket—the old Brown Bess of song and story; 1816 was the year in which George Stephenson employed locomotive power on the Killingworth Railway; Fulton's first steamboat had moved up the Hudson but seven years before Paget's birth, and the first steamboat in Great Britain was seen upon the Clyde but two years previously; twenty-four years were yet to pass before a steamboat would cross the Atlantic. The great John Hunter had been dead only twenty years; Malthus was preaching his doctrine of overpopulation; the War of 1812 between the United States and England was not concluded; James Madison was President of the United States; Thomas Jefferson and John Adams were still living; Benjamin West, the artist, was at the height of his fame; Charles Dickens was two years old. The achromatic microscope had not been invented; auscultation and hypodermic medication had not been devised; anæsthetics and antiseptics had not been thought of; modern chemistry had scarcely been born; physiology was still but an unimportant division of medicine, and had not been erected into a separate science by the genius of Magendie and Müller. Ten years before, Bichat had founded the science of histology, and the practice of medicine still consisted largely in copious blood-letting and the administration of drastic purgatives.

Paget was educated in Yarmouth. He was a born lover of nature, and even at an early age was a student and observer. He was particularly interested in botany, and when a mere boy contributed to a book a section on Entomology, describing insects and the plants on which they live and feed; and he also wrote *The Natural History of Yarmouth*. Paget was apprenticed to a surgeon for four years, and then entered as a student in St. Bartholomew's Hospital. He became a member of the Royal College of Surgeons

in 1836. He never had the good fortune to become a house surgeon, and this he always greatly regretted; but he worked faithfully in the dispensaries, and was for some time clerk in the medical ward. He was accompanied by that common companion of genius—poverty—and added to his small income by teaching French and German, which he had studied assiduously. In 1843 he was appointed a Fellow without examination; and in 1849 was made Demonstrator of Morbid Anatomy—a new branch, in those days just beginning to receive recognition. He also lectured on physiology, which up to his time had been taught as a subsidiary branch of medicine, one teacher giving the lectures on both subjects. Paget's lectures drew large crowds, in spite of the fact that they were given at nine o'clock A.M.; and they were charming in their clearness, directness, and simplicity. His appointment as Lecturer to the Royal College excited some resentment, on the ground that a boy had been sent to teach them; but a single lecture served to justify the selection. In 1844 he became Curator to the Museum of the Royal College of Surgeons, and catalogued it with rare carefulness and ability.

From this time on he came to various great dignities: President of the Royal College of Surgeons, of the Pathological Society, of the Clinical Society, and of the Medico-Chirurgical Society; Vice-Chancellor of the University of London; Member of the Institute of France; Fellow of the Royal Society; Sergeant-Surgeon to the Queen. In 1871 he was made a baronet by Mr. Gladstone.

From his school-days in Yarmouth to the termination of his life he was always plain, modest, unassuming, and simple-hearted. He hated notoriety, and the admiration of the vulgar throng was a thing that he neither looked for nor desired. He was never a stickler for personally obtaining credit—and a man can do a great deal of good in this world if he is not particular who gets the credit for it. He was vastly ignorant of many things which command the interest of multitudes of men; for instance, the famous jockey Archer, who once came to take advice, was greatly amazed to learn that Paget had never even heard his name. He rose above petty strifes and mean contentions as the mountain rises above the lightning and the storm. He was not great in public

and small in private life, as is not unusually the case with distinguished men; neither was he noble in important matters and mean in small ones. Not a few notable men have had opposite characteristics and have resembled the thunder, mighty and magnificent, which yet stoops to sour the milk in a poor man's larder. Temptation never allured him, even when it came dressed in the garb of opportunity. He pursued, unflaggingly, the best of all life's quests—the benefit of humanity—and he pressed the rich grapes of splendid talent into the goblet of noble desire. As one who has written of him says, his was “a life devoted from first to last to the highest objects,” and its most conspicuous feature was “moral greatness.” (*The Practitioner*, February 7, 1900.) He was an indefatigable worker and a painstaking, careful, and brilliant observer. He believed in observation at first hand and in taking nothing for granted, and always held Hunter's view, as shown in his letter to Jenner. Jenner had theorized about smallpox, and Hunter had written him, “Do not think, but investigate and know.” Paget was born at a time when theorizing was extremely fashionable, but he lived to see the spirit of investigation displace it, and came to be a leader in the revolution. (*The Practitioner*, article above quoted.)

He was one of the first and one of the very best of those modern scientific surgeons who have employed the microscope to investigate the problems of disease. (*The Practitioner*, February 7, 1900.) He was that rare combination—an anatomist, a physiologist, a pathologist skilled in the use of the microscope, a diagnostician, a teacher, and an operating surgeon.

He spoke frequently and always well, and Gross and many others have put on record their admiration for his talents as an orator. He could speak impromptu with a grace and a beauty which charmed his audience. His lectures were intellectual treats, clarified, explained, and fortified by excellent blackboard sketches made by himself. His more finished addresses, it has been said, were committed to memory; but they were delivered with such ease that they gave the impression of unstudied force rather than of careful elaboration. (*The Practitioner*, February 7, 1900.) Many of his lectures and addresses have been published. He did an

enormous amount of literary work, and in our library can be found over forty of his productions.

Paget's most notable book is *Lectures on Pathology*. This is a medical classic, and, in spite of numerous changes of opinion, it will always be read, like Watson's *Practice of Physic*, Trousseau's *Clinical Lectures*, Stokes on *Fever*, and Hilton on *Rest and Pain*. Among his other writings we may mention *The Catalogue of the Museum of the Royal College of Surgeons*, *Lectures on Tumors*, *Lectures on Inflammation*, *The Morton Lecture on Cancer*, and particularly the *Clinical Lectures and Essays*. This latter book should be read by every surgeon. It is filled with striking, instructive, and original observations; and its absolute truthfulness is one of its most notable elements. This work contains the famous essay on "The Calamities of Surgery," and in it he fearlessly details some of his own failures and mistakes. Paget's writings are not filled with ponderous references and manifold quotations, but are original studies and observations—a rare merit in this age, in which so many books, like so many plays, are merely adapted from the German.

As an operator he was certainly successful, but not brilliant. He was accurate, painstaking, conscientious, and always acted with excellent judgment. After the completion of the operation he gave personal attention to the care of the case.

Paget died in London on December 30, 1899, in his eighty-fifth year. He retained his faculties to the last, and at the time of his death stood in the very front rank of the profession. The *London Practitioner* says that he was "A worthy successor of the philosophical school, which includes the names of Cheselden, Pott, Hunter, Cooper, Brodie, and Lawrence—a school that has done so much to raise surgery from a base, mechanical art to a calling that demands the highest qualities of the man, and which by the prompt assistance that it affords in moments of danger, as well as by the permanent benefits that it confers, is of the highest importance and eminence."

Paget was an Englishman, we are Americans; but we claim a place among the mourners at his tomb, for no fame can rise and burn in England but that it reddens these western skies. The lines

which divide us are traced in water ; the bonds which unite us are stronger than steel ; and such men as Sir James Paget do more to bring nations into brotherhood than do sworn compacts and written treaties. He was an Englishman by birth, but he belongs to the Commonwealth of Science : and it is with a feeling of respect, admiration, and affection that we pay this tardy tribute to his memory.

He was a great man, a good man, a gentleman. Peace to his soul !



## MEMOIR OF WILLIAM PEPPER, M.D.

BY JAMES TYSON, M.D.

[Read April 3, 1901.]

FROM a life so crowded with events and so fruitful of important and wide reaching results as that of Dr. Pepper, it is difficult to decide what is suitable for a memoir intended for preservation in the archives of the "College," as well as to be read to its Fellows. For the former, fulness of detail can scarcely be excessive: for the latter, the axe of condensation must prune out much that would add to the interest of a memoir to be read in the closet. Abbreviation may, however, be excused when it is known that there will shortly be published by Prof. Francis N. Thorpe an extended biography which will deal exhaustively with Dr. Pepper's life.

Dr. Pepper's ancestors on his father's side were German. His great-grandfather, Henry Pepper, emigrated from Strassburg to this country so lately as 1739, and settled in Schaefferstown, in what is now Lebanon County, Pennsylvania, removing to Philadelphia in 1774. His father, Dr. William Pepper, was the leading physician and consultant in Philadelphia at the time of his death at the comparatively early age of fifty-four. He was four years Professor of Theory and Practice of Medicine in the University of Pennsylvania, resigning in consequence of ill health. He was especially skilled in diagnosis based on exhaustive and accurate investigation of each case. Dr. Pepper's mother, Sarah Platt, represented the fifth generation in descent from Thomas Platt, whose exact place and date of birth are unknown, though he was born somewhere between 1685 and 1690. His son, Thomas Platt, was born in Burlington County, N. J., in 1715. Dr. Pepper's great-grandfather,

John Platt, was born in the same county in 1749, but moved to the vicinity of Wilmington, Delaware, about 1795, having previously served as Captain in the Delaware Regiment of Foot throughout the Revolutionary War. His son William, Dr. Pepper's grandfather, was also born in Burlington County, but was taken to Delaware when very young. Later he resided in Camden, N. J., and still later in Philadelphia, where his children, including Sarah Platt, were born.

Provost Pepper was born at 1304 Walnut Street, Philadelphia, August 21, 1843. His youth was spent in Philadelphia and at his father's country-seat in Chestnut Hill. He was educated altogether in Philadelphia, first at St. Mark's School attached to the Parish of St. Mark's P. E. Church, the Head-master of which was Rev. Ormes B. Keith, who still lives in New York City; and later at the well-known Classical Academy of the late Rev. John W. Faries, where he was prepared for the College Department of the University of Pennsylvania. He entered the University in September, 1858, and was graduated Bachelor of Arts, July 3, 1862, receiving the degree of A.M. in Course in 1865.

His career in college was suggestive of the brilliancy of his later life. He was president of his class, was always an honor man, being valedictorian, or second honor man, at graduation, Charles C. Harrison, the present Provost of the University, being the first honor man and salutatorian. He was awarded the Senior English Prize, and equally with the late Prof. John G. R. McElroy the "Philosophy Prize." He was a member of the Phi Beta Kappa Society, the members of which, it is well known, are selected from those of highest standing in each class. He was also a prominent member of the Zeta Psi, University of Pennsylvania Chapter.

The following are among the more prominent members of his class at graduation:

Rev. Jesse Y. Burk, the present Secretary of the Board of Trustees of the University of Pennsylvania.

John Cadwalader, Collector of the Port of Philadelphia, 1885-89, etc.

Rev. George Stuart Chambers, D.D., a prominent Presbyterian Clergyman of Harrisburg, Penna.

Thomas Mutter Cleemann, a civil engineer of prominence in this country and in South America.

Dr. Persifor Frazer (D. Sci. Nat. of France), Professor of Chemistry, University of Pennsylvania, 1870-74; same at Franklin Institute, 1881-93; and same of Pennsylvania Horticultural Society, 1889 to date; Geologist, etc.

Charles Custis Harrison, the present Provost of the University of Pennsylvania. (See *Alumni Register*, July, 1900.)

Rev. John Sparhawk Jones, D.D., one of the Chaplains to the University of Pennsylvania. A prominent Presbyterian clergyman in this city.

Captain Robert Patton Lisle, Pay Director United States Navy.

The late Prof. John George Repplier McElroy, Professor in the University of Pennsylvania, 1869-90.

The late Thomas McKean, Trustee; munificent donor to the University of Pennsylvania.

The late Dr. George Pepper, Dr. Pepper's dearly beloved brother.

Rev. Robert Ritche, of the Protestant Episcopal Church.

Skipwith Wilmer, a distinguished lawyer of Baltimore.

Immediately after his graduation in "Arts," he began the study of medicine with his father, then residing at 1215 Walnut Street. He entered the Medical School of the University of Pennsylvania in the fall of 1862. The Professors were Samuel Jackson, Hugh L. Hodge, Joseph Carson, Joseph Leidy, Robert E. Rogers, Henry H. Smith, and his father, Dr. William Pepper. He received his diploma March 12, 1864, by which time Drs. Jackson and Hodge had been succeeded by Drs. Francis Gurney Smith and R. A. F. Penrose. The subject of his thesis was: "Movements of the Iris and Some of Their Relations." Although we attended lectures together for one term, 1862-63, I saw little of him at that time, and we first met at the Pennsylvania Hospital in July of the latter year, when I became resident physician at the hospital. Dr. Pepper, then a student of medicine, substituted Dr. John Conrad, the hospital apothecary, who was taking his annual vacation. We were room-mates. Here began an acquaintance later ripening into a friendship which continued until his death. Our colleagues at the hospital were Dr. Thomas Hollingsworth Andrews, who was substituting Dr. William Savery, and Dr. Horatio C. Wood, the medical resident. I had myself been elected to fill the unexpired term of Dr. Joseph C. Richardson, resigned. The characteristics I recall of Dr. Pepper during this month or more of our residence at the hospital were his cheerful, hopeful disposition, his enthusiasm and his alertness. He never loitered, and whether it was in the despatch of his duties as

apothecary, or off to the river in the afternoon for a row, he always moved quickly and gaily. He read rapidly and omnivorously, and among the books he read I remember George Johnson's then comparatively new work on *Diseases of the Kidney*. During the succeeding winter of 1863-64 he was a regular attendant on the clinics at the hospital, and I recall him vividly, bounding up and down stairs, two and three steps at a time, to and from the clinics.

In consequence of the precarious state of his father's health, Dr. Pepper did not enter a hospital as resident physician immediately after graduating, but as soon as practicable after the elder Pepper's death, which occurred October 15, 1864, he became resident at the Pennsylvania Hospital, and served from April, 1865, until October, 1866. It was during this time that he formed his friendship with Dr. Edward Rhoads, whose lofty character and great ability were lost to the profession after a brief but promising career. Dr. Rhoads was my class-mate in the medical school and succeeded me at the Pennsylvania Hospital. During this association Dr. Pepper and Dr. Rhoads studied together the minute changes in the blood in malarial fever, and later published a paper on "The Fluorescence of Tissues," in the *Pennsylvania Hospital Reports* for 1868, and in the same volume another on "The Morphological Changes in the Blood in Malarial Fever," in connection with Dr. John Forsyth Meigs. These papers were based upon the study of 123 cases of a severe form of bilious fever which occurred in the service of Dr. Meigs in the summer and autumn of 1865, and involved much physical and chemical research and a large amount of microscopical investigation. The object of the paper on "The Fluorescence of Tissues" was to show that a substance found in the normal tissues by Bence Jones which possessed a property of fluorescence like quinine and called by him "animal quinioidine," disappeared under the influence of the malarial poison.

Immediately after leaving the Pennsylvania Hospital, Dr. Pepper began practice at 1215 Walnut Street, having been elected Curator and Pathologist, March 26, 1866, some months before the expiration of his term as resident. On January 28, 1867, the Managers granted him the use of a room in the Picture House on Spruce Street in which to give a course of lectures on pathological anatomy. In 1867 he

was elected Pathologist to the Philadelphia Hospital, and in the same year one of its visiting physicians. In 1868 he was made Lecturer on Morbid Anatomy in the University.<sup>1</sup> He prepared while Curator a descriptive catalogue of the pathological specimens in the Museum of the Pennsylvania Hospital, covering 138 closely printed octavo pages, based on one previously made by Dr. Thomas G. Morton. As Pathologist to the Philadelphia Hospital he was the first to arrange the making of autopsies with a fixed hour for each day, and gathered materials and drawings for his lectures at the University. He devoted himself with his usual enthusiasm to his wards and to teaching in the Philadelphia Hospital until his extensive practice and absorbing public duties forced him to resign November 24, 1884, having resigned the position of Pathologist to the Pennsylvania Hospital in 1871.

In 1870 he became Lecturer on Clinical Medicine in the University of Pennsylvania, and in 1876 professor of that branch,

<sup>1</sup> In consequence of this appointment he gave only one or at most two courses on pathology. The lectures on morbid anatomy at the University were given in the autumn course preliminary to the winter course by a corps of lecturers, consisting of Drs. Hayes Agnew, on Regional Anatomy; James J. Levick, on Physical Diagnosis; H. Lenox Hodge, on Diseases of the Skin, in addition to Dr. Pepper on Morbid Anatomy and myself on Microscopy. Before the course began (September 7, 1868) Dr. Levick was replaced by Dr. Edward Rhoads. Dr. Pepper was made Lecturer on Clinical Medicine in 1870. Dr. Rhoads died in January, 1871, when Dr. Pepper was assigned to Physical Diagnosis and Clinical Medicine, and Dr. Joseph G. Richardson to Morbid Anatomy. Dr. Hodge, who had succeeded Dr. William Hunt as Demonstrator of Anatomy, replaced Dr. Agnew, who had become Professor of Clinical and Demonstrative Surgery, and Dr. Harrison Allen replaced Dr. Hodge as Lecturer on Diseases of the Skin. These constituted the lecturers in 1871. Dr. Allen gave the lectures on skin diseases for one year only, and was succeeded in 1872 by Dr. Louis A. Dubring. In 1873 this Spring Course was further enlarged by the addition of lectures in Practical Chemistry by the then Prof. R. E. Rogers, on Diseases of Women and Children by Dr. William Goodell, on the Eye and Ear by Drs. William F. Norris and Strawbridge, and on Surgical Diseases of the Mouth by Dr. James E. Garretson. The lectures were the last given in the old University buildings in Ninth Street above Chestnut. The next regular Winter Session of 1873-4 was given in the building of the Pennsylvania College, 250 Ninth Street; that of 1874-5 was the first delivered in the New Medical Hall in West Philadelphia. In the spring of 1874 the lectures were given in the same building, beginning March 30th, and extending through April, May, June and September by the same men, Dr. Agnew having become Professor of Surgery in the Medical School. On the completion of the Hospital in West Philadelphia in 1874, a Hospital Staff was appointed, which included these men, in addition to the Professors of Medicine, Surgery, and Obstetrics, a Clinical Professor of Nervous Diseases, who was Dr. H. C. Wood, and a Professor of Clinical Surgery, Dr. John Neill. Dr. Tyson's title was changed to Clinical Lecturer on Pathological Anatomy and Histology. In point of fact, Drs. Stille and Penrose, who were *ex-officio* members of the staff, never gave lectures in the Hospital. Drs. Garretson and Richardson were not included in the staff. April 4, 1876, Drs. Neill, Goodell, Pepper, and Tyson were made members of the Faculty, the title of Dr. Tyson's chair being changed again to General Pathology and Morbid Anatomy.

holding this position until 1884, when he was chosen Professor of Theory and Practice, to succeed the late Dr. Alfred Stillé. In the meantime, in 1881, he had become Provost of the University, retaining this office until 1894.

Dr. Pepper took an active interest in many of the medical societies of his city, state, and country. Naturally the Pathological Society was his first field, as it was that of Gross, of Stillé, of Da Costa, and of Ashhurst. He became a member in 1865, and at once its leading member. He was chosen Vice-President in 1870, and was its President from 1873 to 1876. He was made a Fellow of the "College" in 1867, and immediately took an active part in its proceedings. His most important papers were "Trephining in Cerebral Disease," read May 18, 1870; "The Internal Use of Nitrate of Silver," read May 7, 1877, and "Addison's Disease," read January 7, 1886. In addition to these papers, his remarks on the communications of other Fellows were always full of valuable information, gained largely from his own experience. Thus succeeding a paper read by J. Ewing Mears on "Encysted Dropsy of the Peritoneum," although Dr. Pepper had only been eleven years in practice, he cited three cases of the comparatively rare condition which had occurred in his own experience. Thus it was with every subject which came up when he happened to be present. In consequence of the exacting demands on his time by the numerous and important interests in which he was concerned in recent years, he was compelled, much to his own regret, to neglect the meetings of the "College," but he always took a warm interest, and I know from personal knowledge, looked forward to the time when, freed of some of his responsibilities, he might again contribute to its proceedings and take a hand in its management. It was through his instrumentality chiefly that in 1870, three years after his election to Fellowship, the "College" for a time increased its meetings to two a month, with the idea that one meeting should be devoted to scientific matters only and the other to business. At that day, however, the number of Fellows was much smaller and there was much less activity among them, so that the semi-monthly meetings could not be kept up. Quite recently, when it appeared to some of us that the time had come for the formation of a Section on Medicine for the purpose of

stimulating this department. Dr. Pepper attended the meeting for organization in January, 1897, though he was at the time overwhelmed with work and broken in health, and had not for a long time attended a similar meeting. This was the last meeting of a medical society he ever attended.

He was one of the founders of the Obstetrical Society in Philadelphia, in 1869, but was never active in its work, as he never practised midwifery. He became a member of the Philadelphia County Medical Society in 1871, of the American Medical Association in 1872, and of the Medical Society of the State of Pennsylvania in 1875, and in the early part of his career was a frequent contributor to their *Proceedings*. He delivered the address in "Medicine" before the State Medical Society at its meeting in Pottsville in 1875, which at once charmed and astonished the older members, for he was then but thirty years of age. He was chairman of the Committee of Arrangements of the American Medical Association at its meeting in Philadelphia in 1876. He was one of the founders of the Climatological Society in 1884, and its President in 1886; also one of the founders of the Association of American Physicians in 1886, and its President in 1891. He was the first President of the Pan-American Medical Congress, at its organization in Washington in 1893, and delivered an able and most impressive address, which was listened to with rapt attention by a large audience made up of delegates and their friends, from Mexico, South America, the West Indies, Canada, and the United States. Its subject was "The State of this Continent and its Original Inhabitants at the Time of its Discovery by Columbus, and the Obstacles which Opposed Him and the Great Men who Completed His Work," together with "The State of Medical Science in Europe at the Time of the Discovery and the Spirit which Controlled its Subsequent Course." It abounds in valuable information, involving laborious historical research, gathered and collated at a time when he was excessively busy. It excited the enthusiastic admiration of the representatives from British and Spanish America, which was reflected in the reception given him in the City of Mexico at the second triennial meeting of this Congress in 1896. The Pan-American Congress itself owes its existence to Dr. Charles A. L.



Reed, of Cincinnati, who introduced a resolution creating it at the meeting of the American Medical Association at Washington, May 5, 1891. Dr. Reed was made chairman of the preliminary organization. In the fall of 1891 Dr. Pepper was unanimously elected President, and Dr. Reed was chosen Secretary-General of the first Congress, which it was decided to hold in Washington, D. C. Dr. Pepper threw himself energetically into the work and was instrumental in securing an appropriation from Congress toward the expenses of the meeting. At its inception he had few sympathizers, but, like all else he undertook, he made the Washington meeting a magnificent success, as the two splendid volumes of nearly 1200 pages each, which contain the *Transactions* published in English and Spanish, abundantly attest. They include a vast amount of information bearing on medicine from all parts of North and South America which could in no other way have been accumulated. Dr. Pepper remained Chairman of the International Executive Commission, which is the permanent body of the Congress, until his death. As Chairman of this Commission he attended the second Congress, held in the City of Mexico, November 15-19, 1896, delivering an address in the National Theatre on the evening of November 16th. He received much attention while in Mexico, and was especially honored by President Diaz. A fitting termination of the relation established with Mexico was a memorial meeting, held September 12, 1898, in the City of Mexico, in the National Chamber of Deputies. President Diaz presided, while about him were gathered cabinet officers and other government officials, the principal citizens, scientists, and physicians of the republic. The first address was by Hon. Matias Romero, the Mexican Minister to the United States, who eulogized Dr. Pepper as an altruist who had sacrificed himself for the good of his fellow-men. Dr. Porfirio Parra spoke, in behalf of the National Medical School, of Dr. Pepper's medical life; Dr. Arellano, in behalf of the Board of Health, of his social and humane qualities, and Dr. Mendizabal concluded by a glowing eulogy, in which he summed up Dr. Pepper's life work. The occasion was rendered more impressive by appropriate music.

Among the first of Dr. Pepper's important objects was the founding, in 1870, of the *Philadelphia Medical Times*. He secured a



guarantee fund, chiefly from members of the profession, from which was made up for three years any loss sustained by its publishers. The first number was issued October 1, 1870. First a semi-monthly, it became later a weekly, and although it has been discontinued for some years, the journal contained the best literary productions of such men as S. D. Gross, Alfred Stillé, D. Hayes Agnew, John Forsyth Meigs, J. M. Da Costa, R. J. Levis, William Goodell, Addinell Hewson, James H. Hutchinson, John Ashhurst, Jr., Harrison Allen, S. W. Gross, Frank Maury, John S. Parry, George Pepper, William Pepper, and others who have passed over into the unknown country. An examination of the early volumes shows that its publication marks an era in the medical activity of Philadelphia, whence we may date the extraordinary development of medical education which has characterized the last thirty years of the century just closed. Dr. Edward Rhoads was to have been the editor, but his failing health permitted only the preparation of the first number. I have elsewhere said that Dr. Pepper edited the journal for two years, and am sure he edited it for several months, but was surprised on taking down the first volume to find that the editor was James H. Hutchinson and associate editor James Tyson. I had forgotten how close was my own relation to the journal.

The removal of the *Medical News* to New York, in 1896, left Philadelphia without a first-class medical weekly journal. Dr. Pepper felt this was a serious deficiency in a city which had always taken such a prominent position in matters medical, and was restless under this feeling. Early in the fall of 1897 he began to organize a company for the purpose of establishing a journal which would fill this gap. With his usual broad and liberal views, he sought to interest not one, but all the medical schools of Philadelphia, and not only succeeded in this, but secured also the interest of prominent business men other than publishers of medical books, including those of large experience in the management of successful newspapers. By October 1, 1897, the arrangements were completed, a Board of Trustees appointed, and George M. Gould appointed editor, with an Executive Committee representing all interests to co-operate with him. On Saturday, January 1, 1898, appeared the first number of the *Philadelphia Medical Journal*, which promptly established itself

in the front ranks of the medical journals of the world, and by its example has elevated medical journalism in America to a plane it would not have reached for many years, if at all.

The first of the enduring works of Dr. Pepper, characterized by its magnitude and importance, was the founding and completion of the Hospital of the University of Pennsylvania. Initiated by a committee from the Society of the Alumni of the Medical Department, March 14, 1871, on the motion of Dr. William F. Norris, it involved securing from the city at a nominal cost a tract of land worth at least \$200,000, an appropriation of \$100,000, and again \$100,000 from the State, in addition to the raising by subscription of \$350,000 for endowment, and was completed in its first stage by appropriate ceremonies of inauguration held at the Hospital, June 4, 1874.

Subsequent stages included the addition of the Gibson Wing, rendered possible by the generosity of the late Henry C. Gibson, stimulated by the persuasion of Dr. Pepper, whose efforts also secured a liberal endowment for the same; the Maternity Hospital and Agnew Pavilion, in behalf of the latter of which he again successfully invoked the aid of the State, while his own purse completed the conditions that made it possible.

The Hospital had barely reached the first stage of its completion before another permanent institution of great and growing importance received his attention—the Pennsylvania Museum and School of Industrial Art—and I well remember the bright afternoon in June, 1875, when we parted at the railway station in Pottsville, he to return to Philadelphia to take part in the first meeting for the organization of the Museum, and I to the sessions of the State Medical Society, which were not yet concluded. He did not, however, continue long associated with it, and went on the Board of Trustees for only one year, finding himself deeply involved in work, much at this time growing out of his appointment as Medical Director of the International Exposition, commonly known as the "Centennial," which was to be opened in Philadelphia the next year. He supervised the sanitary arrangements of the Fair and organized a medical corps for the treatment of emergencies. For his distinguished services in this connection he was decorated by the King of Sweden Knight

Commander of the Order of St. Olaf, and received recognition also from the English Government.

At this time (1876) the Medical Faculty of the University was enlarged by the addition of Professorships of Clinical Surgery, Clinical Medicine, Clinical Diseases of Women and Children, and General Pathology and Morbid Anatomy, to which Drs. John Neill, William Pepper, William Goodell, and James Tyson were respectively appointed. Simultaneously the important step of prolonging the Medical Course from two to three years was also under consideration, and in it Dr. Pepper was naturally most active. The plan was consummated early in 1877, and inaugurated by his notable address, delivered October 1, 1877, entitled "Higher Medical Education the True Interest of the Public and the Profession." Closely followed the foundation of the Dental Department of the University, in 1879, and the construction and furnishing, at a cost of \$90,000, of the Laboratory Building, in which were accommodated the Laboratories of Chemistry and Dentistry and the Dissecting-room. The Veterinary Department of the University was established through his efforts in 1884, and in the same year the Biological School and the Course Preparatory to Medicine in the College Department.

The Laboratory of Hygiene was conceived by him, and though rendered possible by the munificence of Mr. Henry C. Lea, his influence with Mr. Lea went far to secure it, while the conditions of the latter's gift involved the raising of \$200,000 for endowment, also collected through the efforts of Dr. Pepper. It was completed in 1891. Close on this followed the prolongation of the Course in Medicine from three years to four, and the magnificent gift of \$50,000 to secure its consummation. The Wistar Institute of Anatomy, the gift of General Isaac Wistar, General Wistar himself tells us, was the result of conviction through Dr. Pepper's efforts that it would serve a useful purpose in the teaching of anatomy and the development of anatomical knowledge, as well as a storehouse for the famous museum inaugurated by his distinguished ancestor, Dr. Caspar Wistar. It was commenced June 10, 1892, and finished May 3, 1893. These acts, more particularly associated with the medical department, culminated in 1895 with the erection and partial endowment of the William Pepper Labora-

tory of Clinical Medicine as a memorial to his father, Dr. William Pepper, and his brother, Dr. George Pepper.

The handsome and commodious Library of the University of Pennsylvania was built under the inspiration of Dr. Pepper from plans by Frank Furness, with a capacity of 275,000 volumes within its fire-proof walls. It is equalled by few college libraries of the world, and compares well with many municipal and national library buildings. The corner-stone was laid October 15, 1888, and it was completed during the summer of 1890 at a cost of \$200,000, largely aided by Dr. Pepper's efforts. It was formerly opened to the public Saturday, February 7, 1891.

Some allusion should be made to Dr. Pepper as an author and a teacher. Reference has already been made to many of the papers and addresses which he prepared. Among others should be mentioned papers on "Phosphorus Poisoning" and "Variola," published in 1869; "Tracheotomy in Chronic Laryngitis," "Abdominal Tumors," "Trephining in Cerebral Disease," and "Progressive Muscular Sclerosis," in 1871; "Local Treatment of Tuberculous Cavities" and "Operative Treatment of Pleural Effusions," in 1874; "Sanitary Relations of Hospitals" and "Progressive Pernicious Anemia," in addition to the address before the State Medical Society, already mentioned, in 1875; "Cheyne-Stokes Breathing in Tubercular Meningitis," in 1876. In 1883 he read one of his most noteworthy papers before the State Medical Society at its meeting in Norristown. It was entitled "A Contribution to the Clinical Study of Typhlitis and Perityphlitis." In it he first called attention to the *relapsing feature* of appendicitis, and reported several cases. Although the importance of early surgical treatment was not appreciated at that day, and although prolonged medical treatment was recommended where at the present day surgical interference would be promptly made, the present practice was foreshadowed in the following paragraph: "The operation is so simple, and, if properly performed, so free from danger and complications, that it is to be hoped that hereafter the indications for its performance will be more clearly recognized and more constantly borne in mind, not by surgeons only, but by the general practitioners under whose care such cases come, and by whom the necessity for the operation must

be recognized, even if they prefer to call in a consulting surgeon for its performance." The following paragraph points in the same direction: "It is not too much to say that the unjustifiable delay permitted in many cases of typhlitis, while hoping day after day for the more definite detection of suppuration, is the direct cause of many avoidable deaths."

In 1870 was published his revision of John Forsyth Meigs' work on *Diseases of Children*, long familiarly known as Meigs and Pepper on *Children*. In 1886 he published, in connection with Guy Hinsdale, *A Climatological Study of Phthisis in Pennsylvania*. He is widest known as an author from his editing *A System of Medicine by American Authors*, better known as Pepper's *System of Medicine*, published in 1885, one of the most successful publications ever issued from the American medical press. He wrote the articles on "Catarrhal Pneumonia" and "Relapsing Fever," for the study of which in Philadelphia he had peculiar facilities in 1866. Pepper's *Text-Book of Medicine by American Teachers* was published in 1893-94, and was immediately successful.

As a teacher, Dr. Pepper's greatest power lay in the clinical lecture. He was rapid in his examination of a case, quickly recognized distinctive features, and promptly drew conclusions; was at times almost intuitive in his diagnosis, a great contrast in this respect to his father, who was a laborious and exhaustive investigator who seldom erred. In addressing students he was impressive and authoritative, and they as well as patients remembered what he enjoined. His prescriptions were simple, but his directions were explicit and emphatic. As a practising physician he was hopeful and encouraging, according to the views of some too much so; but his encouraging opinions were the natural result of his hopeful nature and not assumed. He could not take a discouraging view of anything. They served to make the last hours of many a poor sufferer comfortable and tranquil, although they sometimes sorely disappointed afflicted friends.

On the 22d of April, 1894, I received the following short note from Dr. Pepper:

"DEAR T.: The winter's work has been so hard that I cannot bring myself to face another like it. Everything is in good shape, and I pro-

pose, therefore, to cut the Gordian knot to-morrow, and want you to have early information of it.

Yours sincerely,

"W. P."

On the next day he sent to the Board of Trustees his resignation of the Provost's office, from which I extract these paragraphs:

"With deep thankfulness I recognize that the University has reached a stage of development and prosperity which justifies me in laying down the high office you entrusted to me more than thirteen years ago, and which I held so long as it was possible to combine the administrative labors of Provost with the demands of medical teaching and practice. This time has now passed, and I beg therefore to tender my resignation, to take effect after the coming Commencement.

"The close of the coming session will witness the completion of the formative period of the University. From a group of disconnected schools there has been gradually organized a great academic body, complete in its unity and instinct with varied yet harmonious activities. Mutual confidence and co-operation have developed a system strong enough for effective central control, yet so flexible as to admit affiliation with many separate organizations.

"To our University is due the credit of establishing university extension in America, yet the important and successful society which controls this movement has no organic relations with the University, save that the Provost is *ex-officio* the Honorary President."

Some idea of what was accomplished during the period of his provostship may be gathered from the following:

In 1881, when Dr. Pepper became Provost, its property was fifteen acres: at his resignation there were owned or controlled by it, in a continuous tract and solely for educational purposes, not less than fifty two acres. The value of the lands, buildings, and endowment in 1881 was estimated at \$1,600,000; in April, 1894 it was over \$5,000,000. Prior to the date of the late Henry J. Towne's bequest the University had never received a single large gift or legacy. During the year ending September 1, 1894, there were acquired in lands, buildings, money, and subscriptions not less than \$1,000,000. The members of the teaching force in 1881 numbered 88, and the students in all departments 981; at the date of his resignation the former were 268 and the attendance had reached 2180, representing every State in the Union and no less than thirty-eight foreign countries. The College Department had attained a national distinction.

The Medical School had been advanced to pre-eminence in equipment and prosperity, while plans were maturing destined to place it abreast of the great schools of Europe. The Law School had effected a prolongation and elevation of its curriculum, and had acquired a national reputation, while progress had been made toward providing a magnificent building, which has since been completed. The Dental and Veterinary Departments were in successful operation and plans for their further development were matured. The Department of Philosophy had been organized in 1884, and had 154 students, extending the privileges of the University to women on equal terms with men. The necessity of dormitories to the highest development of the University had been recognized, and their ultimate erection was assured.

Dr. Pepper had resigned the provostship, but not to rest. His restless energy knew no bounds, and is well expressed by his own motto—*Repos ailleurs*—rest elsewhere. No sooner had one undertaking been accomplished than another was launched, another, and another. Four of these needed his developing guidance a while longer, and were fortunate to receive it as long as required. They were the Department of Archæology and Paleontology of the University of Pennsylvania, which he had created in 1891, and of which he became President in 1894; the Museum of Science and Art; the Commercial Museums of Philadelphia, and the Free Library. It is impossible in a memoir like this to give an adequate idea of the labor involved in maturing these projects. I saw much of him and thought myself familiar with his work, but had no conception of its extent until after his death.

The picturesque and imposing Museum of Science and Art was his conception, and was rendered necessary to house the rapidly-growing collections of the Department of Archæology and Paleontology. Originally a complete museum building was projected to cost only \$150,000, but at Dr. Pepper's suggestion a plan for a more extensive and more imposing structure was adopted. The completed scheme involves a building to cost from \$2,000,000 to \$2,500,000, including an imposing dome, which forms a natural completion to the present wing. The cost estimated of the dome alone is \$125,000. The building, so far as constructed, was built



at a cost of \$385,000, and Dr. Pepper himself was the largest subscriber after the State of Pennsylvania, which appropriated \$150,000. It was not finished until after his death, and was formally opened with appropriate ceremonies December 20, 1899, at which time also the monument of Dr. Pepper was presented to the University. It was cast in bronze from designs by Karl Bitter, and stands on a pedestal designed by Leigh Hunt, on an elevated portion of the grounds adjoining the Free Museum, overlooking many of the buildings which his energy and generosity created. On the same occasion his widow, Frances Sergeant Pepper, presented \$50,000 as an endowment for the William Pepper Hall of the Museum. In behalf of the precious collections themselves, his efforts were untiring and extended. As President of the Department of Archaeology and Paleontology, he established relations with other institutions—with Harvard University, the Smithsonian Institution and Bureau of American Ethnology at Washington, the Egypt Exploration Fund and the Egypt Research Society in England. The Presidency of the Pennsylvania Branch of the Archaeological Institute of America and the founding of the American Exploration Society, the influencing of legislation of the city and State and national legislatures, the securing of land and the raising of lavish sums of money for the furthering of exploration were all conditions of success in the great movement. All these he undertook and accomplished.

The idea of the Commercial Museums of Philadelphia originated with Prof. William P. Wilson, who was sent by the City of Philadelphia to the World's Fair in Chicago in 1893, commissioned to lay the plans of the institution before the ambassadors, ministers, and representatives of the foreign countries there exhibiting. Dr. Pepper was, however, early conferred with and promptly threw his whole soul into the work, giving several hours daily for many weeks. The result was not only a museum of the kind described, but "an organization most complete and systematic for the distribution of commercial information and the methodical study of universal commerce." It involved extensive relations with government officials and the representatives of foreign nations, including the organization and guidance of an International Congress. To the success of these



measures the fascination of manner and energy of purpose which always characterized him contributed greatly.

It is not impossible that, measured by its far-reaching influence and the breadth and depth of the intellectual development it fosters, the Free Library of Philadelphia may become the greatest of all the monuments to his zeal, his energy, his inspiring example. "A library in which every man, woman, or child of proper age can have as ready access to its books as they can have to the few volumes stored upon the shelves in their own homes," he said, "is a necessity." For this he secured legislation from city and State providing for its growth and support. For this he not only secured priceless gifts of books and money, but also convinced the rich that it was their privilege to devote their wealth, and even costly residences, to the service of this magnificent purpose. For this on Sunday afternoons and evenings, as well as on weekdays amid his multifarious engagements, he addressed in different parts of the city interested gatherings of men and women. For this and like objects also he sacrificed his life on the altar of his splendid purposes.

It was Dr. Pepper's habit to cast about him for the public work which most needed stimulating, devoting his attention to it until it was thoroughly on its feet and then passing on to another. Had he lived, the Philosophical Society, to which he was elected in 1870, would certainly have profited by his touch, he having been chosen Vice-President in January, 1896. The historic College of Physicians, under the lead of Stillé, Agnew, Weir Mitchell, and Da Costa, did not require his efforts, and he wisely directed them elsewhere.

Evidences of failing health presented themselves even prior to the winter of 1896-7, when he had one or two attacks of grippe, which always affected him severely, and he was compelled to go South for a time to secure needed rest. In the summer of 1897 he went to California and was absent for two months, during which he greatly improved and returned refreshed and invigorated. He plunged actively into work, the Loan Bill and legislation in behalf of the Free Library claiming much attention, in addition to the work of the Museums and the demands of his large consulting and office practice. Early in January, 1898, he had an attack of influenza associated

with serious bronchitis and troublesome cough. This prostrated him greatly, and although he improved enough to go to work for a little while, he soon broke down again, and after he had improved sufficiently to do so, went South for several weeks. He returned benefited, but with health still shattered. During the month of June, 1898, he was far from well, but kept more or less at work in spite of several anginoid attacks. His family were at Bay Head, N. J., but he could not remain there. His precordial oppression seemed worse there. There was sometimes edema. Once he went to New York City, hoping that at the top of one of the many-storied buildings he would be more comfortable. I saw him last in July, 1898. I was coming out of my house when he drove up and sprang lightly from his carriage, just as he did when in perfect health. We walked together up Spruce Street, chatting and joking, until we arrived at the corner of Eighteenth, when he left me, gaily running across the street to his house. He could never go slowly. This was our last meeting. On the 7th of July he left for California, and was very ill on the day of his leaving. He had an obstinate spell of vomiting in his office and reached the train with difficulty. In Chicago he was desperately ill. Dr. Alonzo Taylor, who was with him, told me he thought he would die at his hotel. By the free hypodermic use of strychnine and digitalis, however, he was tided over this danger and crossed the mountains safely to the home of his friend, Mrs. Phebe A. Hearst, where he died suddenly in an attack of angina July 28th. He had been reading Stevenson's *Treasure Island*, and died with a copy of the book in his hand. He would have been fifty-five years old on August 21st.

An autopsy was made, for the record of which I am indebted to Dr. Alfred Stengel. The valves of the heart were healthy, but the coronary arteries were in an advanced state of sclerosis with consequent disease of the myocardium. The right coronary was almost completely occluded at one point by an area of especially intense disease and by a partially organized thrombosis within. There was some atheroma of the aorta and of the general arterial system throughout the body. The liver was highly sclerotic and the kidneys showed the effects of the cardiac failure, being swollen and highly degenerated. The apex of the left lung was greatly puck-

ered and retracted, and embedded in the fibrous tissue which caused the contraction were found several small cheesy foci. These were undoubtedly remains of the tuberculous infection from which he had suffered many years before, and which was thus evidently wholly cured. The arteries of the circle of Willis were sclerosed and calcified in a most remarkable manner. Several of the branches were almost completely occluded and none of them was seemingly of more than half its previous or normal calibre. There was no gross change in appearance in the cerebral substance. The brain was considerably above the average in size."

More useful than to relate the events of a life, however important these, is it to picture the qualities which lie at the foundation of its success and constitute the spring of its actions. What was it in Dr. Pepper that made him what he was, that secured his success in organization, in financing, and in originating and completing great and useful undertakings? First of all, his undying hopefulness and his unwearying energy, which, as I have said, knew no bounds, scarcely knew fatigue, and were never discouraged by defeat. Defeat he met, but never discouragement, while the bitterness of heart which so often follows it found no place in him.

Of undoubted influence also was his refined and inspiring manner, which attracted all who fell within his influence. About five feet ten inches in stature, of late years he had a slight stoop, which was not ungraceful; his prominent nose did not detract from his handsome face and winning smile. His habit was, especially at the first meeting, to look at one with raised eyes, continuing his gaze intently for a short time. His ability to enlist the interest of others lay largely in these qualities, which were increased by an earnest persuasive speech and a gentle voice. He has been well characterized as "delicately aggressive."

His power of rapid thought and prompt conclusion greatly facilitated his conduct of affairs and enabled him to consider two or three matters at one time, though he sometimes gave offence in this way to individuals who considered they should have his undivided attention. Some of his most important plans were evolved under such circumstances.

Another factor which contributed to his success was his own personal liberality in fostering the projects he started. He himself had simple tastes, and, although he provided himself with all that was necessary to enable him to take care of his health while travelling, he was simple and unostentatious in his habits. But he gave liberally of his means to public undertakings, and by his example stimulated others to a like liberality. He sought profitable investments and worked hard in his profession to make money, but it was not for himself that he did it. It was in order that he might lay it out for the advantage of others. He is said to have given nearly half a million dollars of his own earning to the various institutions in which he was interested, and to have raised ten millions more. He secured from the City of Philadelphia, at one time or another, a hundred acres of land in what will probably ultimately be the heart of the city.

It was impossible for a man of Dr. Pepper's far-reaching activity and success to be without enemies and detractors. Causeless hostility and detraction arise variously in accordance with individual traits, the sum of which constitute the opposite of magnanimity. Such persons may be haunted by imagined wrongs or aggrieved by disappointed expectations and baffled efforts. Some are more or less the critics of all who succeed, others of those whose methods do not concur with their own. The deportment of Dr. Pepper to his enemies was one of the most distinctive features of his character. An eminent writer said of him: "No characteristic of this extraordinary man is more prominent than his genius for treating enemies like friends. Seldom has a man been born into the world so free from the capacity for jealousy, envy, hatred or malice."<sup>1</sup> This is strictly true. I never knew him to speak an unkind word of one of his enemies. He acted as though unconscious of their efforts, while fully aware of them. The importance of such qualities to one who is constantly originating great undertakings which require the influencing of legislation and the reconciliation of opposite factions is evident. It is so natural to feel aggrieved and resentful, for a time at least, under disappointment and unfair dealing, that extenuation

<sup>1</sup> Francis Newton Thorpe, in "A Remarkable American," *Century Magazine* for February, 1901.

may be allowed. Extenuation was not, however, necessary in his case; he was so entirely free from resentment.

It is difficult at so early a date after death to place a correct estimate upon the importance and usefulness of any life, and it is perhaps better always to defer the effort at such an estimate until time has eliminated all personal relations by the death of friends and critics alike. If we look around us, however, at the institutions which originated through his efforts, or developed through his touch from their original beginnings, the most conservative judgment must admit that his name should be linked with that of Benjamin Franklin, Benjamin Rush, Robert Morris, and Stephen Girard as eminent benefactors of his native city.

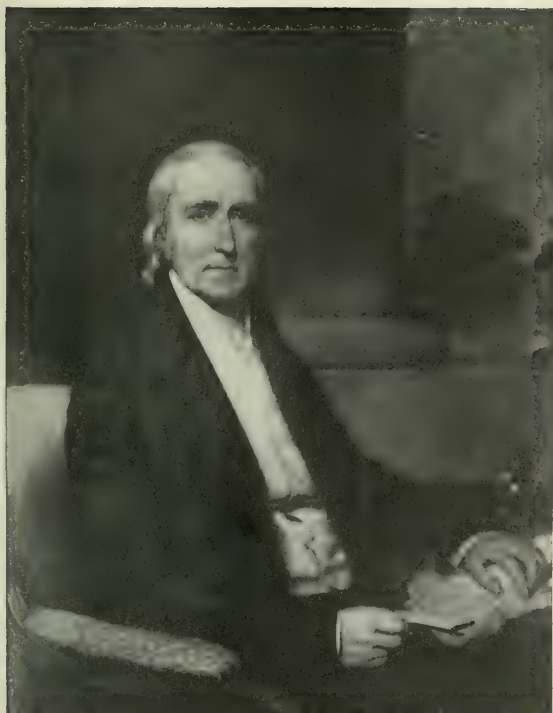
## AN ANALYSIS OF THE CHARACTER OF DR. PHYSICK.

By GEORGE McCLELLAN, M.D.

[Read October 2, 1901.]

DR. PHILIP SYNG PHYSICK was one of the men whose justly earned fame added lustre to the city of Philadelphia and laurels to the Medical Department of the University of Pennsylvania over one hundred years ago. I take this opportunity of referring to some of the traits which obtained for Dr. Physick the rare appreciation and recognition during his life, which was epitomized in the title of "Father of American Surgery," conceded to him by his friends and enemies alike. Dr. Physick was born in Philadelphia, at Third and Arch Streets, in 1768. He enjoyed a liberal education in his youth, and matriculated in the study of medicine at the University of Pennsylvania, in 1786, under the preceptorship of Dr. Adam Kuhn.

It was required of him that he should diligently read the entire works of those masters in the profession whom his preceptor considered infallible, and Dr. Physick appears to have committed the greater part of these works to memory. The effect which this effort produced upon his mind was a singular one, because, after he entered upon the practice of his profession, he was forced to unlearn and to endeavor to forget many of the teachings which these books contained, as experience showed him they were futile and impracticable. To this circumstance of his early life may be attributed Dr. Physick's unwillingness to leave behind him any writings of his own. During his pupilage at the University he gave marked evidence of ability, which was characterized by a desire for thoroughness and accuracy of knowledge which attracted the atten-







tion of those with whom he was brought in contact. He did not wait to obtain the doctorate from the University, but opportunity presenting itself to go to England (in 1788), he enrolled himself among the students of the Royal College of Physicians and Surgeons in London, where he graduated with the highest honors in 1791. He visited Edinburgh the following year, and passed the examination in the University there, receiving the degree of Doctor of Medicine. It is interesting to note that while in London he became associated with the famous John Hunter, who took so warm a personal interest in him that he confided many of his investigations to Dr. Physick. At the present day, in the cabinets of the Hunterian Museum, some of the most valuable preparations are the handiwork of Dr. Physick, made under the direction of John Hunter. Also, while Dr. Physick was in London he enjoyed the companionship of Dr. Jenner at the time that he was engaged in the study of smallpox and of his discovery of vaccination.

There is a story told about Dr. Physick soon after he became an interne at one of the London hospitals (St. George's) which illustrates those elements of his character which made it conspicuous throughout his life. A patient who had been admitted with a dislocated shoulder was left to be attended by the younger surgeons. The Englishmen, after loudly proclaiming the advocacy of the different methods then in vogue for reduction of the dislocation, finally turned to the silent young American doctor who was standing by, and said he might have the first chance, expecting little from their rival from the other side of the water. Physick said nothing, but reduced the shoulder with amazing judgment and precision of action, bowed, and left the amphitheatre.

For three years after he returned to Philadelphia (1793-1796), Dr. Physick, according to his own testimony furnished by a friend, did not earn enough from his professional work "to pay for the soles of his shoes." He was not idle, however, for then, as always, there were plenty of the poor and needy who gladly sought his services. Doubtless he was rewarded by the acquisition of knowledge thus obtained, which gained for him much of his future reputation. Certainly he thereby gained the affections of the humbler classes, which vied with those of the richer in that singular demonstration at the time

of his funeral, recorded by contemporaneous writers, as having been one of the most affecting scenes ever witnessed in Philadelphia. In 1793 the first epidemic of yellow fever broke out in Philadelphia, and Dr. Physick had ample opportunity among the poor, who suffered most from the ravages of the disease, to investigate its cause and treatment. This brought him to the notice of Dr. Rush, who was then at the zenith of his fame. At the time it chanced that Dr. Rush had had a misunderstanding with Dr. Wistar, who was then the most prominent surgeon. Dr. Rush, who was not in the habit of undertaking any operation, was obliged, in the circumstances, to seek for some one who would perform for him the work which Dr. Wistar had been doing, and he called on Dr. Physick, to their mutual advantage and benefit. Dr. Physick rapidly acquired not only a lucrative practice, but an enviable position among his confrères. A dispute arose in the profession as to whether yellow fever was or was not contagious. Dr. Physick ventured to make dissections of the bodies of patients who died from yellow fever, and deduced from them and other careful observations his belief that it was not contagious. Dr. Rush at first differed from him, but subsequently concurred in his views. The dissections which Dr. Physick made upon the bodies of those who died from yellow fever led him to recognize the importance of knowledge to be obtained only in this way, and he advocated post-mortem examinations in all cases where the cause of death was not clearly understood. So earnest was he in his conviction of the importance of this means of acquiring definite knowledge, that he not only became the originator thereby of the study of pathological anatomy in this country, but, through the general recognition which the profession gave it, far-reaching results speedily followed.

That remarkable man Napoleon Bonaparte, the truthful history of whose character is only gradually becoming known, and whose "last phases" have been recently given to us by Lord Roseberry, had his attention drawn to the value of pathology through the reports of Dr. Physick's work on yellow fever, and immediately ordered that the physicians in his army should make post-mortems of all soldiers dying of contagious or epidemic diseases.

Dr. Physick's many and valuable original procedures in surgery,

as well as the remarkable capacity for teaching, demonstrated at the Pennsylvania Hospital, gained for him the Chair of Surgery in the University in 1805. He held this chair until 1819, when he was transferred to that of anatomy, which had been occupied by Dr. Dorsey, Dr. Physick's nephew.

At this time my grandfather was a student at the University, and possibly imbibed from the lectures of Dr. Physick some of the earnestness of purpose which led him to undertake the founding of the Jefferson Medical College.

The Chair of Anatomy proved irksome to Dr. Physick, and as he was gradually failing in health, he resigned it and retired from practice in 1827. It was probably about this time that he sought recreation and rest at his country place, Laurel Hill. On his death he bequeathed the house and grounds to his daughter, Sally, who had married his friend and colleague, Dr. Randolph, and from him the house has borne the name of "Randolph Mansion" since.

In judging a man's character by the successes he achieved and the honors he won, how little do we know of the obstacles which he overcame and of the efforts which they required. Throughout Dr. Physick's life there was steadfastness of purpose coupled with a high ideal. Thoroughness in the acquisition of knowledge and conscientiousness in its use led him to the position he attained. His nature was sensitive and proud, but without selfishness or egotism. He was during the long period of his greatest work a sufferer from disease, which he bore patiently and manfully. What a lesson it is when we consider that the last great operation done by Dr. Physick was upon Chief Justice John Marshall. The world took note of the picture, produced by fate, when the greatest of lawyers called on this great doctor to relieve him. But is not the other side of the picture equally impressive? Dr. Physick had at that time become so enfeebled himself that he had abandoned operating, but when summoned he obeyed, and did the work so well that no one observed the strain, and all marvelled at the coolness and skill which saved the patient's life. It should be remembered that ether had not then been discovered and that surgical operations were attended by unavoidable pain, which not only added to the terror of the patient, but of necessity increased the demand upon

the surgeon's powers, and must have severely tried the self-control of a nature like that of Dr. Physick.

Anecdotes are not wanting of his kindliness, humanity, and consideration for those who consulted him. This was conspicuous in a way which ought to be recorded. Dr. Physick is said never to have done an unnecessary operation. His judgment leant upon his conscience, and although his vast knowledge and experience enabled him to dare and do what few others would have undertaken, it is to his lasting credit that he never yielded to the temptation to operate for reward or acclamation. Dr. Physick *dared not to do* ; and for this I honor him. Would that in this respect he had, even now, more followers !

# REPORT OF A CASE OF CHOLELITHIASIS, WITH FORMATION AND RUPTURE OF AN ABSCESS OF THE ABDOMINAL WALL.

By JOHN H. GIBBON, M.D.,

SURGEON TO THE BRYN MAWR HOSPITAL; ASSISTANT SURGEON TO THE JEFFERSON COLLEGE  
HOSPITAL; SURGEON TO THE OUT-PATIENT DEPARTMENTS OF THE PENNSYLVANIA  
AND CHILDREN'S HOSPITALS.

[Read January 2, 1901.]

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THE following case of gallstones is reported because of the interest it holds from a diagnostic and pathological point of view. I first saw the patient on September 26, 1900, with Dr. E. J. Stout, and she was admitted on that day to the Jefferson College Hospital. The history she gave was as follows:

R. S., a widow, aged fifty-three years; housework.

*Family History.* Mother and one sister died of apoplexy. Father died suddenly in his eightieth year. Six sisters and one brother living and well. No history of tuberculosis or malignant disease obtainable.

*Personal History.* Remembers no illness in her youth. Menses always normal. Never had typhoid fever. For the past fifteen years has suffered from dyspepsia.

*Present trouble* began four years ago, when the patient had a severe attack of abdominal pain situated in the right side of the abdomen, low down, radiating to the umbilicus and occasionally to the right shoulder. Since this attack the patient has had many others and has never been entirely free from pain in the lower part of the abdomen on the right side. The attacks lasted two or three days and none were as severe as the first. The patient never vomited, was never jaundiced, never collapsed from pain, and never, so far as she knows, passed any gallstones. On November 6, 1899, she had a severe attack of pain lasting several days, accompanied by chill and fever on the first day and throughout by headache and constipation, but no vomiting and no jaundice. The point of greatest pain was

situated in the right iliac fossa and the trouble diagnosed as appendicitis by her attending physician, a man of ability and large experience. The application of an ice-cap relieved her suffering. The patient recovered from this attack, as from others, but continued to have a dull, aching pain in the right iliac region. Dr. Stout first saw the patient about the beginning of the following summer, when she consulted him for advice regarding a mass which was forming apparently in the abdominal wall over the region of the appendix. She did not appear to be very ill and did not see her doctor with any regularity. About the last of August the mass softened and opened, discharging a small quantity of pus and leaving a sinus, which has remained open ever since.

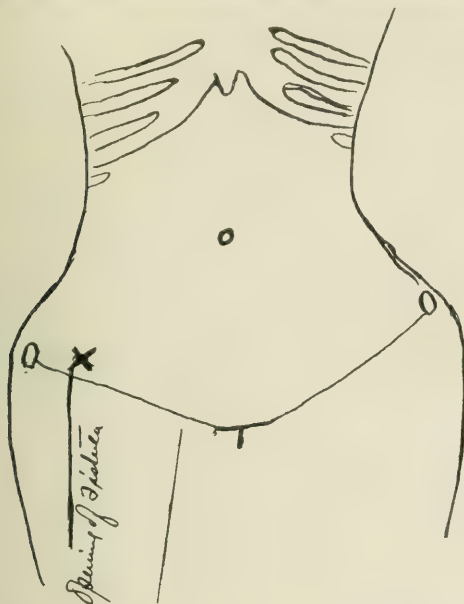
It is interesting to note that when the patient came to Dr. Stout she was wearing a truss, which had been recommended by another physician for the relief of the mass which was supposed to be a ventral hernia.

*On Admission.* Temperature, pulse, and respiration normal; heart and lungs normal. Urine turbid, amber, acid, specific gravity 1021; no albumin, no sugar, urea 1.2, no pus, blood, or tube casts.

Examination of the abdomen showed a small sinus two and a half inches internal to the right anterior superior spine of the ilium and three-quarters of an inch below the level of this spine. Around the sinus the abdominal wall was indurated, red, and tender for a considerable area, so much so as to render palpation and percussion on the right side of the abdomen very painful and of no advantage. From the sinus there was discharged a muco-pus; a bent probe passed into it could be moved about in what seemed a small, irregular cavity, but it could not be passed to any depth in any direction. That there was an abscess of the abdominal wall was apparent, but its cause was obscure. The very positive history of attacks of appendicitis, and the situation of the sinus exactly over the normal position of the appendix, of course made us think of the possibility of this organ being the cause of the trouble; but the character of the discharge and the extensive infiltration of the abdominal wall remaining so long after the opening of the abscess, together with the fact that when rupture did take place there was only a small amount of pus discharged, caused us to put this idea aside and examine in other directions. The possibility of having to deal with a suppurating cyst suggested itself, and also the question of its being a broken-down gumma was discussed. The gall-bladder never entered my mind, because of the patient's history of never having been jaundiced, of always having the pain in the right iliac fossa, of passing no stones after the attacks, together with the diagnosis of appendicitis and the situation of the sinus. The mucous character of the discharge and other facts in the history of the case which were elicited subsequently should have caused us to consider the gall-bladder. I concluded it was an abscess of the abdominal wall and did not think it had any connection with an abdominal viscus. Dr. Stout had already given the patient

iodide; but we decided, that as she had been very irregular in her treatment and because of suspicious-looking scars on her legs, to try increasing doses of the iodide and the local application of mercurial ointment. After about a week it was decided to thoroughly open and curette the abscess.

*Operation.* On making an incision I found an abscess dissecting in several directions and containing about an ounce of pus mixed with a clear, thick fluid. The abscess walls were thick, tough, and smooth. After



curetting thoroughly every pocket I found one in the bottom of the wound that was small and seemed to contain something hard which I could not move. With a hæmostat I dilated the pocket and then withdrew, much to my surprise, a gallstone, and following it fifty-one others. The stones were uniform in size, being a little larger than peas. When I had dilated the opening sufficiently to admit my finger I found that it went not into a sinus leading into the gall-bladder, as I had expected, but at once into the



gall-bladder itself, and I was able to pass the end of my finger into a dilated cystic duct, from which I removed several stones. The peritoneal cavity was not opened. A large drainage-tube was inserted and the patient returned to bed. She reacted nicely, her temperature but once going above 99°, and she went home on the twenty-fifth day, with the wound practically healed. During the first week there was a considerable discharge of bile, which showed the cystic duct to be clear of obstruction, and as no jaundice developed after the external fistula closed we felt assured that the common duct, too, was free. The fistula closed completely soon after the patient went home, but opened again within a few weeks and discharged bile and mucus until recently, when it closed again and has remained so ever since.

**DIAGNOSIS.** The first interesting question which this case suggests is that of diagnosis. Not infrequently there is difficulty in making a differential diagnosis between inflammatory conditions of the gall-bladder and the appendix, and the fact that a number of excellent surgeons have reported cases where they operated expecting to find one of these conditions and, to their surprise, have met the other makes it a matter of importance. The error of diagnosis, however, I think, is often not made from a want of means or symptoms, which would at least suggest a doubt, but rather from a tendency to consider only the prominent symptom and to make a hurried diagnosis. The fact, too, that both the conditions require operation makes us less careful, and we rest with the idea of making a definite diagnosis when the abdomen is opened.

In the case I report, however, I think, from the patient's history, that it would have been difficult to make a correct diagnosis of the attack which she had in November, 1899, everything pointing toward the appendix region and practically nothing suggesting the gall-bladder. It has been shown that gallstones are much more common than is generally supposed, occurring in from 5 to 10 per cent. of autopsies done on Europeans. In a large number of these cases no symptoms were present which pointed to the condition. I suppose that no one will doubt, in the light thrown on this case by the operation, that the patient never had appendicitis, but that what was supposed to be this condition was a displaced and inflamed gall-bladder, which was probably becoming adherent to the parietal peritoneum over the right iliac fossa.



It is, of course, a question whether gallstones were present at this time and whether they might not have resulted from the inflammation, which in its turn was due to the colon bacillus, it having been proved beyond doubt that this bacillus, or most any bacterium, may produce a precipitation of the solids of the bile and the formation of gallstones.<sup>1</sup> It would seem, however, when the previous history is considered, that the gallstones were present at this time and the cause of the inflammation and suffering. I do not think it would have been possible to make a diagnosis of gallstones when the patient was admitted to the hospital in September of this year, for, beside the absence of symptoms, the inflammation and induration of the abdominal wall rendered examination very unsatisfactory. The character of the discharge should, however, have made us suspect the real condition.

**PATHOLOGY.** The first thought in regard to the pathology of this case is the abnormal situation of the gall-bladder in the right iliac fossa. Enormous distention of the gall-bladder is not infrequent, cases having been reported where this condition was mistaken for an ovarian cyst. Robson speaks of a specimen in St. Bartholomew's Museum in which a greatly distended gall-bladder formed the contents of a femoral hernia. Carl Beck reported in the *Annals of Surgery* for May, 1899, an interesting case of transposition of the viscera, in which gallstones developed and were removed through an incision made along the outer border of the left rectus muscle. In my own case it will be observed that there was practically no distention of the gall-bladder and no ptosis of the liver, so its abnormal position must be accounted for in some other way, and I think the correct explanation is a long, peritoneal attachment to the liver. Under ordinary circumstances the gall-bladder is in intimate relation with the under surface of the liver, being kept in this position partly by the peritoneum, which passes from its sides to the liver; but Brewer (*Annals of Surgery*, June, 1899) in examining one hundred bodies found in five that the gall-bladder was completely surrounded by peritoneum which in passing to the liver formed a mesentery, which permitted considerable mobility, and in three cases there was an extension

<sup>1</sup> Mayo Robson: Gall-bladder and Bile-ducts.

forward of the free border of the lesser omentum to the fundus of the gall-bladder.

Robson reports a case (Case No. 234, page 281) which in many respects resembles the one here reported: "Strong family history of phthisis; in twelve months several attacks of severe pain in the right iliac region, accompanied by swelling in the normal situation of the cæcum and marked tenderness between the anterior superior spine of the ilium and the umbilicus; each attack associated with fever, constipation, vomiting, and abdominal swelling, and all signs of local peritonitis over the inflamed appendix. Operation: Incision over the cæcum; viscera matted together by old and recent lymph. After separating the adhesions the gall-bladder was reached at end of projecting Riedel's lobe; muco-pus and several gallstones removed; tumor of cystic duct felt, and on incision it gave the appearance of growth; it, with the gall-bladder and projecting lobe of liver, was removed by means of the elastic ligature." The patient recovered.

Although in a few cases adhesion, ulceration, and perforation into the stomach or bowel have taken place, yet probably in most instances the gallstones produce an empyema which is evident from local and constitutional symptoms. As the organ is usually found in its normal position, adhesion to the pylorus or bowel or to the liver is more frequent than to the parietal peritoneum. This being true, the gallstones are much more apt to find their way into these viscera than through the abdominal wall. When adhesion to the parietal peritoneum does take place and ulceration and perforation follow, an abscess forms and the pus usually works its way along in the direction of the umbilicus, where it is apt to open externally. This may not always be true, however, for many cases are reported where the fistula found its external opening as low down as the symphysis pubis. Adhesion of the ducts and of the gall-bladder itself to the pylorus and duodenum is frequent, as shown by operations and autopsies, and results often in dilatation of the stomach or obstruction of the bowel. Obstruction of the bowel has also been caused by a large stone which has ulcerated its way into the bowel. Ulceration and perforation into the general peritoneal cavity may take place without the formation of

protecting adhesions, as is shown by Case 241 of Robson's series. Robson says that "If the ulceration advances toward the adjoining hollow viscera, stomach, duodenum, or colon, adhesions, as a rule, form and the perforation is effected quietly. In one case of this kind—after a history of cholelithiasis followed by severe stomach symptoms—the gallstones were vomited and complete recovery followed." Cases have also been reported where the gallstones have by ulceration made their way into the pleural cavity and the urinary tract. Occasionally an adventitious sac has been found, formed by adhesions of neighboring parts, containing gallstones and communicating with the gall-bladder by a small opening. There is, of course, the constant danger of rupture of such a sac and the production of a fatal peritonitis. Again, the gallstones have ulcerated into the walls of the ducts and there remained until removed by the surgeon. Death from hemorrhage not infrequently follows operations on the gall-bladder in cases where there has been a long-standing jaundice which has produced an aplastic condition of the blood. In these cases death from hemorrhage has followed perforation of the gall-bladder. About a year ago I saw death occur from continued and persistent oozing of blood from an incision into a gall-bladder very much inflamed and where the patient had long been jaundiced.

**FISTULÆ.** The question of fistulæ, internal or external, after ulceration, and of external fistula after cholecystotomy, is of interest. It seems that from post-mortem observations we must conclude that the fistulæ established between the gall-bladder and the other hollow viscera tend to become obliterated after a time, and this is apt to be true, too, of the external fistulæ produced by ulceration. Fistulæ following operation are not nearly so frequent now as they were before Robson taught us how to avoid them by suturing the gall-bladder to the fascia instead of to the skin, as had formerly been the practice. He reports 189 cholecystotomies with fourteen fistulæ following, but five of these occurred in the first ten cases, where the gall-bladder was sutured to the skin. Since modifying the technique he has not had a single fistula when the ducts have been cleared at the time of the operation. A mucous fistula, of course, indicates an obstruction of the cystic duct.

## DISCUSSION.

DR. JOHN B. DEEVER: I have listened with interest to Dr. Gibbon's cases, and, having seen one or two instances of a like kind, I can appreciate Dr. Gibbon's position when he refused to commit himself as to the cause of the trouble in this particular instance.

It is a very difficult matter to differentiate between certain cases of terminal appendicitis where the appendix "looks upward to the north," as we commonly say, and cases of cholecystitis. I take it that his case was one of calculous cholecystitis. Owing to the obstruction to the cystic duct and the change that takes place with the excretion of the lining membrane of the gall-bladder, in consequence we have abscess of the gall-bladder. I have seen the gall-bladder occupying a position similar to that occupied in the doctor's case. I recall one in particular, and Dr. Taylor no doubt recalls the case, which was in St. Agnes' Hospital. The gall-bladder extended below the anterior superior iliac spine for some distance, well back into the flank. While these cases are very uncommon, yet they excite more or less interest.

There are some points in this case which are of interest—the pain referable to the shoulder, the patient complaining more or less constantly of pain, and presence of chill. In my experience a chill is more common in cholecystitis than in appendicitis. Pain referable to the shoulder is quite common in bile-duct disease. I have operated on close to one hundred cases, either of gallstones in ducts or the gall-bladder, and in many of those cases patients have given a history of chill; the latter is exceptional in appendicitis.

The doctor properly calls attention to death from hemorrhage in neglected gall-bladder cases. My mortality, with one exception, was confined to that lesion—hemorrhage following the operation. I very much dislike to encounter a badly jaundiced patient. It is a character of hemorrhage that may be very difficult to control. I have seen after these wounds are closed continued oozing, until the patients were so profoundly shocked that death resulted. Hemorrhages that have occurred in my cases have been consecutive hemorrhages, those following operation immediately.

Regarding the question of fistula, as Dr. Gibbon has said, we owe the proper technique to Dr. Robson. In my early experience in gall-bladder work I saw more fistulae than I do now. I then stitched the gall-bladder to the skin. I now stitch it to the anterior sheath of the rectus muscle.

DR. RICHARD H. HARTE: I have been very much interested in Dr. Gibbon's paper, and particularly in the discharge which he found coming from the fistula. He spoke of its being serous in character. I think this is very often the case in abscess of the gall-bladder, the purulent matter

rather gravitating to the lower portion, and when first noticed the serous or mucous portions will be found occupying the upper half of the fluid, and after that has been drained off, then the purulent collection has usually been found below. I have noticed this condition in quite a number of cases, and am not at all surprised that Dr. Gibbon was a little misled by seeing the serous discharge at first coming from the opening.

DR. SOLOMON SOLIS-COHEN: Two points in connection with this surgical paper may be commented upon by a physician. First, some of the gallstones passed around are almost white. There must be a number of cases in which, in searching for gallstones in the stools, physicians and patients may be misled through looking for dark objects rather than for light ones. I have had two cases in which white gallstones were passed, and in one of them the objects were so round and smooth that at first they were mistaken for undigested quinine pills. Secondly, I should like to ask Dr. Deaver, and the other surgeons who have been troubled by hemorrhage in these cases, whether they have made use of the recently introduced physiologic styptics—adrenal extract, or adrenalin, or the styptic of Dr. Wright, of Dublin, which latter is composed of thymus extract and calcium chloride. These have proved useful topical agents in controlling hemorrhage, and especially general oozing from other sources than the liver, and perhaps might prove equally useful in the cases described. Calcium chloride may also be given internally for three or four days preceding operation to increase the tendency of the blood to fibrogenesis.

DR. GIBBON: In reply to Dr. Cohen, I would state that Dr. Robson, in his work on *Gall-bladder and Bile-ducts*, mentions the use of calcium chloride and says he has used it to advantage. In every case where the patient had been jaundiced for any length of time he uses this remedy prior to operating.

# THE SURGICAL TREATMENT OF ASCITES DUE TO CIRRHOSIS OF THE LIVER, WITH REPORT OF TWO CASES.

BY FREDERICK A. PACKARD, M.D.,

AND

ROBERT G. LE CONTE, M.D.,  
PHILADELPHIA, PA.

[Read January 2, 1901.]

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THE two cases herewith reported are placed on record because of the fact that they are illustrations of a very common condition treated by a method which may be said to be still on trial. This method of treatment has not been employed with sufficient frequency up to the present time to permit of an accurate estimate as to its value. While in neither of these cases was the result such as was hoped for, it is felt that this is one reason why they should be recorded, inasmuch as it is personally known to us that in other instances cases having an unfavorable result have not been placed on record, and that consequently a just estimate of the advisability of the procedure cannot be made. From a medical point of view these two cases illustrate a common experience in regard to cirrhosis of the liver as it is seen in hospital work—that is to say, cirrhosis of the liver in a late stage, with frequently recurring ascites, whose only help lies in repeated tapplings of the peritoneal cavity.

CASE I.—Henry S., white, aged sixty-three years, an engineer by occupation, an Englishman by birth, was admitted to the Pennsylvania Hospital on August 6, 1900.

The family history showed nothing of importance. He had always been a healthy man, never having had any sickness except an attack of gonor-

rhœa, which was followed by stricture. He has always been a heavy, constant drinker, taking in winter about six or eight drinks of whiskey daily; in summer ten or twelve glasses of beer daily, and occasionally more. For the last five years he has noticed that the abdomen has been swollen, especially in the lower portion. For the five weeks preceding his admission he noticed that the abdomen had been gradually increasing in size until finally he was compelled to go to bed, became unable to eat anything, and later was troubled with shortness of breath and swelling of the legs.

On admission his chief complaint was of abdominal distress, which he said made him feel as though the abdomen was going to burst. He was a fairly well-nourished man, with dry, coated tongue, markedly sclerotic arteries, and a pulse of small volume. The notes on his admission stated that there were present a mitral and aortic systolic murmur, that the lungs were negative, the liver was small and without tenderness, and the spleen negative. The notes in regard to the condition of the abdomen on admission are that the veins are quite prominent and the abdomen filled with fluid to such an extent that it measured thirty-nine and one-half inches at a point one inch above the umbilical level. We were surprised to find this note in regard to the prominence of the veins over the abdomen upon his admission, for when he came under our care on September 1st the absence of venous distention was quite remarkable, in view of the extent of ascites. The legs on admission were somewhat œdematous. Examination of the urine showed that it was dark amber, slightly turbid, with a specific gravity of 1025, was strongly acid, contained no albumin or sugar, and in the sediment a few hyaline and granular casts, free pus, and large squamous cells. In spite of the free use of compound jalap powder, given in gradually increasing doses until he was taking a drachm twice daily, the abdomen continued to increase in size until August 15th, when tapping was necessary, and 215 ounces were withdrawn. Eight days later the effusion was noted as having returned. Eighteen days after this first tapping 296 ounces were withdrawn. On September 17th the liver area was said to extend from the upper border of the sixth rib to the costal margin. The circumference of the abdomen was then forty inches at a point one and one-half to two inches above the umbilicus. An increasing discomfort from distention necessitated a third tapping on September 24th, twenty-two days after the second tapping. At this time 320 ounces were withdrawn, and at the end of the operation, although the fluid ceased flowing, it was evident from the dulness in the flanks that all of the fluid had not been removed. Even five days later it was evident that the fluid was reaccumulating. A fourth tapping was necessitated twelve days later, and on this occasion 317 ounces of clear fluid were withdrawn. Owing to the fact that in spite of all care the patient was steadily losing ground, and that tapping at progressively shorter intervals was necessary, it was evident that nature was doing little to obviate the results of portal stenosis, and that no adequate attempt was



being made at an establishment of the collateral circulation through the systemic venous system. On this account it was considered that the case was one adapting itself to surgical intervention, particularly because the condition of the kidneys seemed to be rather unusually good for this class of cases, and, while the arteries were sclerotic, the heart itself showed no evidence of being in bad condition to withstand operative interference.

*October 13th.* Ether narcosis. Abdomen opened in the median line above umbilicus, for a distance of three and a half inches. No adhesions present. Liver inspected and felt, and proved to be firm, smooth, dark, and much reduced in size, with a small amount of fibrous tissue visible. A small incision was then made through the skin and fascia in the middle line above the pubes, and an ovarian cyst evacuator was forced into the abdomen and guided to the space between the bladder and the rectum. A rubber tube had previously been attached to the evacuator, which drained into a bucket. The patient was then raised by the Trendelenburg table to a semi-sitting position, in order that the ascitic fluid might gravitate to the pelvis while the evacuator siphoned it off. While the fluid was draining off the rest of the operation was being carried out. The peritoneum was glistening, not thickened, but much congested and full of minute blood-vessels. The spleen was enlarged to probably three or four times its normal size, with a thick capsule. The surfaces of the liver, spleen, and omentum and the parietal peritoneum coming in contact with these organs were then rubbed with gauze sponges. This rubbing produced a slight hemorrhagic oozing. The omentum was attached to the abdominal wall in two or three places with catgut sutures and the abdominal wound closed. A glass drainage-tube was then inserted in the opening above the pubis, sterile dressings applied, and broad straps of adhesive plaster were made to encircle the abdomen from the lower border of the sternum to a little below the umbilicus. The amount of fluid recovered measured 330 ounces. The head of the patient's bed was raised so that all fluid might drain to the pelvis. The operative recovery was uneventful. The drainage-tube drained a little over a pint of fluid a day.

*15th.* Rubber drain substituted for the glass drainage-tube.

*20th.* Drainage reduced to four or five ounces a day. Tube removed but tube-tract continued to ooze.

*24th.* Patient very much depressed. Appetite fair and general condition fair, but weak.

*27th.* Drainage wound closed. Cutaneous veins of abdomen becoming more prominent. Sitting up in wheel chair.

*November 1st.* Mental depression continues; more marked some days than others. Excitement never present.

*5th.* General condition does not seem to improve; is quite weak; appetite variable.

He was readmitted to the medical ward on November 14th. During his



stay in the hospital there was no albumin in the urine and the specific gravity was always fairly well maintained. On his readmission the kidneys were apparently doing their work well so far as chemical and microscopical examination showed. The quantity passed in the twenty-four hours was decidedly below normal. He looked thin and pale, with a typical hepatic facies. The most marked change in his condition as compared with that before the operation was the entire absence of fluid in the abdominal cavity, so far as could be determined by physical examination.



In addition to that there were seen on the anterior surface of the abdomen three large venous trunks. (See figure.) One of these ran from the wound above the umbilicus to the costal margin at the tip of the ninth rib, and seemed to fill both from above and from below upon making pressure on it. Another large trunk ran from the lower portion of the wound to the middle of Poupart's ligament on the left side, and a third corresponding to this on the right side of the abdomen; both of the latter veins filled from above. After his admission to the medical ward he failed to gain very materially, and quite steadily lost ground. Increasing asthenia with cardiac weakness,

which progressed in spite of stimulation, led up to his death from heart failure and pulmonary cedema on December 5th.

At the autopsy, which was performed by Dr. Meigs, at that time on duty in the ward, and by him kindly reported to us, the following conditions were noted:

The abdomen was distended and flabby; the examination was limited to an abdominal incision six inches in length. A certain amount of yellowish fluid slightly tinged with blood was present in the abdominal cavity. The abdominal contents were adherent above and below the umbilicus and toward the left side to the parietal peritoneum.

The anterior surface of the liver was adherent to the abdominal wall by firm adhesions. The omentum lay above the umbilicus and was adherent to the liver. Universal adhesions were found between the diaphragm and the liver, the adhesions being firmer on this surface than anteriorly and inferiorly. The spleen was very large and weighed twenty-one ounces, about three and one-half times its natural size; its capsule was much thickened, its surface rough and uneven after detachment from the parietes. On section the pulp was found to be soft, with some increase in the fibrous trabeculae. The kidneys were normal in size, but on section showed a proportional reduction in the cortex. The liver was small, weighing but two pounds and two ounces. The hepatic substance was torn anteriorly and superiorly where adhesions had been present. The surface of the organ was but slightly uneven in feeling and in color; the right lobe was very much more contracted than the left. On section the parenchyma did not grit under the knife, but there was evident increase in fibrous tissue, with some fatty change. In the portal vein there was found a softened clot occluding the lumen by about one-third its diameter. The umbilical vein was found to be patulous. The heart was of about normal size, but weighed eleven ounces. Marked dilatation of the arch of the aorta at its commencement, with many calcareous plates, was found. The aortic and mitral valve leaflets were thickened. The apices of both lungs were dark and nodular, and both organs were intensely congested and cedematous.

CASE II.—An ex-policeman, James P., aged fifty-two years, was admitted to the Pennsylvania Hospital on September 7, 1900. His father died from cause unknown to the patient; his mother died of "dropsy," as did also one sister. Three brothers and three sisters were living and well. Ten or twelve years ago he began passing blood from the bowel, and occasionally has done so ever since that time. These hemorrhages became troublesome two or three months before his admission. He gave a distinct history of syphilitic infection and confessed to the abuse of alcohol. Four or five weeks before his admission his legs began to swell, and shortly thereafter increase in the size of the abdomen was noted. The latter had been

progressing steadily since then. On examination there were found slight cyanosis of the finger-tips, tortuous temporal arteries, and dilated venous radicles of the cheeks and nose. Anteriorly pulmonary resonance was normal, but when in the recumbent position the note became flat over the region posterior to the anterior axillary region on the right side. This dulness was found to shift with change of position, and over it there was constantly absence of breath-sounds, with diminished vocal resonance and fremitus; otherwise the lungs showed nothing abnormal. The apex-beat was in the normal position, and the cardiac dulness began at the lower border of the third rib and the left parasternal line. No abnormal sounds were heard except for a very faint systolic murmur at the aortic area, which was not transmitted. The abdomen was tremendously distended, and there was found an easily reducible umbilical hernia of the size of a small apple. Two inches above the umbilicus the circumference of the abdomen was forty-four inches. The flanks were perfectly flat, as was most of the surface of the abdomen except for a clear, tympanitic area surrounding the umbilicus. Fluctuation-wave was easily detected. In addition to his umbilical hernia he had a large, left-sided scrotal rupture. The legs were cedematous and their veins somewhat distended. The urine had a specific gravity of 1027, was acid, contained no albumin, sugar, or casts. Three days after his admission six ounces of blood were passed from the rectum, and on the following day he had a slight epistaxis. On September 11th the abdomen was tapped and 346 ounces of clear yellow fluid were withdrawn. The tapping gave a great deal of relief, the abdomen being found to measure five inches less in circumference as compared with the previous measurement. After removal of the fluid, liver dulness was found to begin at the upper border of the sixth rib and to extend downward to the costal margin. On "jogging-palpation" a mass was felt in the upper zone of the abdomen, extending transversely from the ninth costal margin of the right side to the median line about two or three inches below the left costal margin. Four days after the tapping (September 15th) movable dulness was again detected in the flanks, which in two days had increased and distention of the abdomen was becoming manifest. In spite of various plans of treatment the fluid accumulated to such an extent that it was thought that this patient also was a proper subject for operative interference. Consequently the patient was transferred to the surgical ward.

*October 13th.* Ether narcosis. The same surgical procedures were followed as detailed in the last case. The liver was enlarged, hard, and nodular, with a thick, rounded edge. Peritoneum also congested, but not thickened. Spleen not enlarged, so its surface was not irritated. Three hundred and twenty ounces of ascitic fluid recovered. Slight shock following operation, but reaction good. Tube drained about a pint in the first twenty-four hours.

*15th.* Tube draining less than a pint. General condition good.

16th. Slight delirium during night; tried several times to get out of bed; no rise of temperature; mental confusion present this morning and conversation at times incoherent; urine lessened in amount.

17th. Very active and noisy delirium during night, followed by stupor at 2 A.M., which rapidly deepened into coma. Urine very scanty, containing much albumin and casts. Despite free purgation, sweating, and treatment directed toward stimulating urinary secretion, our efforts were unavailing, and the patient died at 10 P.M. No signs of infection were at any time demonstrable, and the cause of death appeared to be uræmia. Post-mortem examination was refused.

A glance at the urine records made while he was in the medical ward shows that there was no albuminuria and no casts in the sediment, and that the urine had a high specific gravity. It is to be noted, however, that the quantity of urine passed in twenty-four hours prior to his admission to the surgical ward never exceeded thirty-four ounces. At the time these observations were made it was thought that the diminution in the quantity of urine was accounted for partly by the frequent occurrence of watery bowel movements, partly by the rapid accumulation of fluid in the peritoneal cavity, and partly, also, by his diet, which was somewhat limited in the hope of causing absorption of the ascites. Owing to the absence of autopsy it is, of course, impossible to state the condition of his kidneys, yet from the evidence afforded by chemical and microscopical examination it would have been supposed that his kidneys would have stood the strain of an operation involving so little as did this one.

From the account of the surgical treatment it will be seen that in both cases it was found at operation that the condition suspected before opening the abdomen was present—that is to say, the absence of adhesions and of any evident attempt on the part of nature to obviate the effects of portal obstruction. In the patient who died shortly after operation it was unfortunate that no autopsy could be performed, so that the anatomical results of the operation must still remain in doubt. In the second case the autopsy, performed sixty-one days after the operation, shows that the results aimed at (the formation of adhesions and the establishment of a collateral circulation) were quite well obtained. What effect the operation may have had in this case in lengthening or shortening life it is difficult

to estimate, as the patient was losing ground before operation, and the very nature of the case would not allow of any estimate in regard to the probable course had no interference been attempted. He died, as do other cases of advanced cirrhosis of the liver, with evidence of a progressive toxæmia and gradual failure of all the organs to do their proper work.

Doubtless one of the ways by which repeated tapplings may aid in the recovery of cases of cirrhosis of the liver is through the formation of adhesions similar to those aimed at in the operative procedure, but to a less degree. The occurrence of ascites in cirrhosis of the liver is undoubtedly a bad prognostic omen. It is, in the first place, a visible measure of the extent of portal obstruction, and, in the second place, it is an indication of a lack of a sufficient attempt on the part of nature to compensate for this obstruction by the establishment of a collateral circulation. The frequent occurrence of cirrhosis of the liver without ascites is well known. Lange (*Inaugural Dissertation*, Kiel, 1888) found ascites present in 34.4 per cent. among fifty-six cases of cirrhosis of the liver of varying degree. Presumably it was absent in the other 65.6 per cent. of the cases. While there are no figures at hand which go to prove it, it is reasonable to believe that in some cases ascites fails to occur because of the establishment of a collateral circulation between the portal and systemic venous systems. While in all cases of cirrhosis of the liver the exact part played by this lesion must be in doubt because of the wide-spread changes present in other vital organs, and probably in all of the tissues of the body, it is reasonable to infer that one of the chief factors in producing a fatal result is progressive toxæmia due to the failure of the liver to destroy toxins absorbed from the portal area. This toxæmia from absence of antitoxic action of the liver is probably present in cases both with and without the formation of a collateral circulation, the only difference between the two classes being that in the former case toxins normally carried by the portal blood would be thrown in large amount into the systemic venous system through the collateral branches directly communicating with the portal supply; whereas in the latter case these toxins would presumably, in part at least, be contained in the ascitic fluid and be removed by tapping.

One of the most exhaustive articles upon ascites and its prognostic value is that by W. Hale White (*Guy's Hospital Reports*, 1893, vol. xlix., p. 1). Some points are brought out in this paper which deserve notice in connection with our subject. Of fourteen cases in which tapping was necessary because of ascites, sufficient data to accurately determine the interval elapsing between the occurrence of ascites and death were found in twelve. This period averaged only sixty-three days. The author makes the additional statement that he has not been able to find a single case among those which he has collected in which any end but a speedy death could be anticipated after ascites had once developed. In ten cases in which paracentesis was not performed the time from the beginning of the enlargement of the abdomen up to death averaged about two months. He considers that paracentesis is of doubtful value in alcoholic cirrhosis of the liver, as he found that in fourteen cases the patient survived the first and only tapping from but two, at the least, to about forty days at the outside. He considers that where ascites is survived for any great length of time some condition other than cirrhosis, or in addition to cirrhosis, is present, or, in other words, that the ascites is not in this case due simply to cirrhosis of the liver. As an instance of this he notes ten cases regarded during life as cirrhosis of the liver, but which were found after death to have some additional lesion which he believes may have had an important bearing upon the occurrence of ascites. All of these except one were instances of chronic peritonitis or perihepatitis. The only exception was a case of colloid cancer of the peritoneum. Among four cases which he relates where tapping had been performed more than once, cirrhosis was absent in three and present, to a slight extent, in one. In all four there was chronic peritonitis, and among six other cases which were tapped more than once there was cirrhosis of the liver with associated chronic perihepatitis and peritonitis. It would seem, then, from these cases related by Hale White, that the presence of a chronic peritonitis and perihepatitis with cirrhosis of the liver has a favorable rather than an unfavorable bearing upon the prognosis, inasmuch as these cases with peritoneal adhesions and thickenings live for a sufficiently long time to make repeated tapplings necessary; whereas in cirrhosis of the liver uncomplicated by



these inflammatory lesions death occurred either before tapping had been required or before a second removal had been practised. It is possible that the longer life after the appearance of ascites in Hale White's six cases of cirrhosis of the liver with chronic peritonitis and perihepatitis was due not to the fact that the ascites was produced by the chronic peritonitis and perihepatitis, but because the effects of cirrhosis of the liver as regards the portal system were obviated by the formation of peritoneal adhesions somewhat similar to those aimed at in Talma's operation.

An interesting case somewhat bearing upon this question was reported by R. L. MacDonald (*Medical News*, October 12, 1889, p. 398). This case was apparently cured, after sixty tapplings, with the removal of an aggregate of 9000 ounces. After an interval of four years from the last tapping the patient was still in good health. In the same paper he records a second patient wherein cure resulted, although at one time it was necessary to remove the ascitic fluid once every three weeks. Altogether thirty-one aspirations were performed, by which from 8600 to 9000 ounces had been removed. At the time when he was last seen, about a year after first coming under observation and six months after the last tapping, the fluid had not reaccumulated. Owing to the fact that both patients recovered it is impossible to say to what the cure must be attributed; possibly compensatory dilatation of the systemic venous trunks obviated the results of portal obstruction, but it is impossible to say whether the repeated tapplings had anything to do with this formation of a collateral circulation.

Quincke (*Nothnagel's spec. Path. u. Therap.*, Band xviii., Theil 1) refers briefly to a case reported by Casati where ascites disappeared after 111 punctures. Quincke states that the relief from the establishment of a collateral circulation rarely becomes sufficient to cause the disappearance of ascites. He gives the average duration of life after the establishment of cirrhosis at ten years. He states, however, that he does not believe the establishment of a collateral circulation can contribute much to the relief of an obstructive ascites, but that when an outspoken ascites disappears it is because chronic peritonitis has had a part in its production. Possibly the same remark might hold good here as was made in regard to Hale

White's observations, namely, that in the cases of cirrhosis of the liver with chronic peritonitis the survival for a considerable length of time was due to the fact that the latter lesion assists in some way in the formation of a collateral circulation.

*History and Theory of the Operation.* To Talma, of Utrecht, belongs the credit of first suggesting the operative formation of adhesions between the abdominal organs and the parietes for the cure of ascites due to cirrhosis of the liver. As a result of this suggestion three operations were performed in Holland; the first, in 1880, by Van der Muele, the patient speedily dying from shock; the second by Schelkly, in 1891, in which the patient on the fourteenth day, during violent delirium, tore off his dressing and infected the wound; death from peritonitis speedily followed. The third by Thomas Lens, in 1892. This case survived the operation, but died in six months without diminution in the ascites. The failure of the improvement was attributed to the smallness and atrophic condition of the liver. Such poor results seem to have had their effect on Continental surgeons, for no further operations were undertaken for four years.

In the meantime Drummond and Morison independently conceived the same idea as Talma, and in 1894 and 1895 Morison operated on two cases in England. In the first patient the diagnosis is in doubt, as the liver at the time of operation showed no evidence of cirrhosis. The patient died nineteen months after operation without any diminution in the ascites. In the second case the liver was typically cirrhotic, the ascites disappeared, and the patient was well two years later. To Drummond and Morison must be given the credit of being the first to bring the operation to a successful issue, and by their success to have brought the procedure prominently before the medical world.

The operation was designed on the theory that ascites in cirrhosis of the liver is due to obstructed portal circulation—*i. e.*, to the increased pressure in the portal vein. If, therefore, some of the portal blood could be made to go directly into the systemic circulation without passing through the liver, the pressure in the portal vein would be relieved and the ascites would disappear. Several cases of cirrhosis of the liver (such as those mentioned above) have



been reported in which, after repeated tapings, the ascites has permanently disappeared, and in one case the patient lived twenty years, death resulting then from causes unconnected with the liver. Post-mortem examination of several cases of cirrhosis of the liver where ascites was absent seemed to show one of two things: either that the viscera were connected to the parietes by vascular adhesions, or that the normal communications between the portal and systemic veins were greatly increased in capacity. These normal communications are: a vein in the round ligament of the liver connecting the left branch of the portal with the epigastric and other veins in the abdominal wall; veins in the subperitoneal tissue lying between the folds of the hepatic ligaments connecting the portal trunk with the phrenic vein and vena azygos major; the coronary veins communicating with both the azygos veins through the œsophageal plexus; the inferior mesenteric vein communicating with the iliac by means of the middle and inferior hemorrhoidal plexuses. The pancreatic veins can also empty into the retroperitoneal veins.

Talma has lately reported three cases in which a natural collateral circulation was evident. All were subjects of cirrhosis of the liver, and at one time ascites had been present, but had disappeared before death. One died of acute bronchitis, the second from a stab wound of the abdomen, and the third from toxæmia due to a progression of the disease. At the autopsies an abundant collateral circulation through enlargement of natural channels was easily demonstrable. In one case the vein of the round ligament of the liver was as large as a finger.

An enlargement of this collateral circulation may sometimes be seen during life in the superficial veins running through the abdominal wall, and occasionally by the formation of a "caput medusæ" at the umbilicus. When these communicating veins enlarge a very considerable amount of blood may be thrown directly from the portal into the systemic circulation without passing through the liver. If these veins do not enlarge, or increase so little in size as to afford little or no relief to the portal congestion, new channels may be formed by adhesions between the viscera and the abdominal parietes. Such adhesions will develop innumerable little vessels, which will enlarge and carry a considerable amount of blood, if they

are needed in economy. We have all seen repeatedly the enormous veins that will form in the omentum when it becomes adherent to large tumors of the uterus or ovary, and the free communication these vessels have with the new growth.

Drummond and Morison therefore reasoned that if the mechanical theory of ascites in cirrhosis of the liver is correct, the establishment of a new accessory circulation between the portal and systemic systems would cure the ascites, and so remove one of the chief causes of suffering and death in this disease.

There are, however, some who object to the mechanical assumption of the ascites on the ground that it does not occur when the blood-pressure is presumably highest in the portal vein—*i. e.*, early in the course of the disease, when hemorrhage from the stomach and bowels are met with—but believe that ascites is a later manifestation of the disease as a result of the toxæmic condition of the blood. This toxæmic state depends upon the cirrhotic liver being unable to destroy the poisons that are continually passing to and from the alimentary canal, and these poisons, reaching the general circulation, exert a lymphagogue action and lead to œdema of the feet, ascites, etc. They therefore urge that the formation of an artificial collateral circulation, while it may modify portal engorgement, would not tend to improve the general state of health, but rather the reverse. However, if such a collateral circulation does lead to improvement, the improvement might be explained in two ways: 1. By diminishing the flow of blood through the liver it may enable the liver to deal more efficiently with the blood that passes through it, and so reduce the toxæmic condition. 2. The increased vascular supply to the surface of the liver may enable the hepatic cells to undergo compensatory hyperplasia by improving their nutrition. The compensatory hypertrophy of the liver will enable the organ to carry on more efficiently its important functions, and so lead to a latency of its symptoms.

In refutation of this latter theory, namely, that the ascites is due to the toxæmic condition of the blood, we would advance the following argument: 1. The hemorrhages from the stomach and bowels in the early stage of the disease do not necessarily prove that the pressure in the portal vein is then at its highest, as they also may be accounted for in nature's attempt to increase the collateral circula-

tion by enlarging the œsophageal and hemorrhoidal plexuses, such enlarged vessels having less resistance to the pressure than normal ones. 2. The lymphagogue action of the toxæmic poisons in the general circulation should exert such action wherever the general circulation goes, and we should have, beside œdema of the legs, œdema of the hands, of the face, of the brain, etc., effusions within the pleura, pericardium, and membranes of the brain, and the most prominent effusion should not be where alone the portal blood exists, namely, the peritoneum. 3. In the first case we reported—a man requiring frequent tapplings for the relief of ascites—artificial adhesions were produced. The man lived two months without a return of ascites, dying as a result of progressive toxæmia. His liver was about half the normal size. If toxæmia had been the cause of the ascites the fluid should have reaccumulated, for he died a toxic death.

We would therefore hold that with our present knowledge as to the cause of ascites in cirrhosis of the liver the mechanical explanation is the best, and that through the relief of the portal congestion, either by the existing channels or by the production of new ones, ascites may be prevented.

The effects of portal blood passing directly into the general circulation have been very carefully studied in a series of experiments in dogs. N. V. Eck, in 1874, conceived the idea of establishing a permanent communication between the vena cava and the portal vein after ligature of the latter at its entrance into the liver. The experiments were very fatal. Of eight dogs treated in this manner seven died within a week, and one, after living two and a half months, ran away and was lost before the effects of the operation could be studied. J. J. Stolnikow repeated Eck's experiments in 1882 with equally fatal results. The post-mortem examination of the liver in his cases showed neither macroscopically nor microscopically any change from the normal. The gall-bladder was filled with bile, the intestines contained bile, and the stools were of normal color. In no case was there any degeneration or necrosis of the liver. This is, of course, natural, as in no case was the nutrition of the liver (the hepatic artery) interfered with. It is interesting to note that bile was still formed, although all portal blood was cut off from the liver.

In 1892 Hahn, Massen, Nencki, and Pawlaw began a similar

series of experiments, and, owing to improved instruments and an antiseptic technique, their results were much less fatal. Of sixty dogs operated upon twenty recovered and were carefully studied. The facts brought out are extremely interesting. A considerable number of dogs showed an immediate change in disposition, which lasted for a longer or shorter period. Gentle and obedient dogs became cross, peevish, and disobedient, and some so fierce that they could not be approached. Stages of excitement and depression followed each other, the ataxic gait was noticed, and stupor, coma, and convulsions were present. Such symptoms were sometimes followed by death, but often the dog entirely recovered. They appeared, as a rule, immediately after operation, but occasionally were delayed for days. The temperature following operation was always subnormal, and the following day it would rise one or two degrees and remain there for ten or fifteen days. Some dogs lost progressively in weight until their death; others kept their weight or even gained. When a dog was fed with meat the above symptoms speedily appeared, sometimes with a fatal result; when fed with non-nitrogenous foods they seemed perfectly well. Such phenomena resemble closely a toxemic or uremic condition in man, and seemed to be the result of nitrogenous foods. The experiments teach us that if portal blood is to be brought directly into the systemic circulation this should be done gradually, in order to avoid an overwhelming toxæmia; and also when a collateral circulation is established, and our patient shows signs of excitement or depression, nitrogenous foods should be reduced or entirely cut off for a period of time.

Tilman undertook another series of experiments on dogs to prove the value of peritoneal adhesions in forming a collateral circulation. He found that dogs in which he ligated the portal vein, or the mesenteric vein before it was joined by the gastric and splenic, died. In one the mesenteric vein was ligated and at the same time the omentum was stitched to the abdominal wall. Death occurred in thirty-six hours. In one the peritoneum was partially stripped from the abdominal parietes and the omentum placed between it and the rest of the abdominal wall; the intestines were at the same time irritated with antiseptic solutions. Eight days later the abdomen was reopened and the mesenteric vein ligated. The dog was very ill with hemorrhages from the bowel. Eight days later he was again re-

opened and the portal vein ligated at its entrance to the liver. Bloody stools again appeared, but the dog recovered. Innumerable small veins became apparent on the abdominal wall. A large hernia developed in the scar of the first operation, which later ulcerated, with profuse hemorrhage. After twelve weeks the dog was killed. The mesenteric vein was changed into a fibrous cord, but the portal vein had not entirely closed, a central channel remaining of the size of a pin-head. There was fatty infiltration of the liver. Such an experiment clearly indicates the possibility of peritoneal adhesions developing very numerous and efficient channels of communication with the systemic veins, and also the value of such communications when the portal system is obstructed. Further proof that such a collateral circulation may be readily produced in man is shown in one of Morison's cases and also in one of ours (the pathological findings are detailed above). Morison's case had been operated upon two years before death for ascites with cirrhosis of the liver. Since then the patient had regained normal health, and death followed an operation for ventral hernia. At the necropsy the liver, spleen, omentum, and intestines were found attached to the anterior abdominal wall, with numerous band-like adhesions. Many of these adhesions seemed to contain little beside bloodvessels, and in several of them the vessels were four inches in length. Some were the size of a normal radial artery.

It has been held by some authorities that improvement in the cases following operation may be due to the simple laparotomy, and they instance the cure of tuberculous peritonitis by such means. Many cases, through mistakes in diagnosis, have had laparotomy performed, and when cirrhosis of the liver was found were closed without further operative procedure. In such cases no benefit was derived from the operation. In a case reported by Talma a simple laparotomy had no effect on the ascites. A little later a second operation was performed and the omentum stitched to the abdominal wall. This resulted in a cure of the ascites.

**THE OPERATION.** A variety of different methods have been used to produce a collateral circulation through peritoneal adhesions. The abdomen has been opened in the median line above and below the umbilicus, in the right semilunar line and on a line parallel with and one inch away from the right costal border. The omentum has

been sutured to the incision alone and to the anterior abdominal wall. The parietal peritoneum has been detached and the omentum sutured between it and the abdominal wall. The omentum has been brought between the liver and the diaphragm and sutured there. The surface of the liver and spleen and intestines has been irritated, and also the peritoneum overlying them. The peritoneal surfaces have been irritated with dull and sharp curettes, with the blade of forceps, with a hat-pin, with finger-nails, and with sponges. Drainage has been used, and, on the ether hand, the abdomen has been closed without it. Ether, chloroform, nitrous oxide gas, and local anaesthesia have all been used. In view of the danger of kidney complications, two cases having died from uræmia, I (Le Conte) would strongly condemn the use of ether.

I (Le Conte) should recommend the following method under local anaesthesia or chloroform narcosis: The incision is made above the umbilicus and a little to the left of the median line, so that no injury may come to the vein in the round ligament. The liver is then inspected and palpated to confirm the diagnosis. A small opening in the median line above the pubis is made, and through this the fluid is siphoned off while the operation above is being completed. The parietal peritoneum over the omentum, liver, and spleen (if the latter organ is enlarged) is dried and gently rubbed with a gauze sponge, the same treatment being also given to the surfaces of the organs. Rougher handling is entirely unnecessary, as a healthy peritoneum when brought in contact with dry gauze for a fraction of a minute will retain the impression of the gauze mesh. The omentum is then stitched in two or three places with catgut to the anterior abdominal wall and the incision closed. If the operation is undertaken in a hospital, where you may be reasonably sure that a drainage-tube will be properly cared for, drainage may be made through the lower opening, particularly in cases where the ascites has been rapidly re-accumulating. If you have no confidence in the nursing, close the lower wound also and resort to tapping until such time as the collateral circulation has been established. Drainage is very useful for three or four days, until the adhesions can become firm. To use it for more than a week seems to be a useless risk to the patient, as a tube tract is probably not formed so quickly as in an ordinary laparotomy, owing to the abundant secretion of fluid, and therefore the



dangers of infection are greater. If the Trendelenburg table is used the patient may be raised to a semi-sitting position while the ascitic fluid is being siphoned off. After the dressing is applied the abdomen should be encircled with broad adhesive straps from the ensiform cartilage to below the umbilicus, in order that the parietal peritoneum may be brought and kept in contact with the visceral. The operation can be quickly finished, and should be scarcely more dangerous than an exploratory laparotomy; but we must remember that other organs beside the liver are frequently diseased (the heart, kidneys, and bloodvessels), and such subjects endure operative interference but poorly.

We have been able to collect from the literature twenty-two cases. Ewart's case has not been added to the table, as the post-mortem proved it to be one of calcareous adherent pericarditis and not one of cirrhosis. A case by Delagénère and two Italian cases have also been omitted, because we have been unable to find any authentic report of their histories or the results of operation, although a cure is said to have been brought about. One case (No. 4) was included, although the diagnosis of cirrhosis was doubtful and was not confirmed at operation.

These twenty-two cases represent all we have been able to gather from the literature on the subject. In what proportion they represent the total number of cases operated upon we have no means of knowing. Small as the number is, it is all we have from which to draw our conclusions. We may look at this table in three ways. Taking all the cases recorded in it we have a total of twenty-two operations, with five immediate deaths (death ensuing from a few hours to fourteen days after operation), three ultimate deaths (the period of life varying from two to nine months, two having no improvement in the ascites and one with the ascites cured), three unimproved, two improved (where the ascites recurred more slowly and in lessened amount), and nine recoveries. Placed in percentages it will read:

Immediate death	.	.	.	.	.	.	22.7 per cent.
Ultimate death	.	.	.	.	.	.	13.6 "
Unimproved	.	.	.	.	.	.	13.6 "
Improved	.	.	.	.	.	.	9.1 "
Recovered	.	.	.	.	.	.	40.9 "

No.	Date.	Operator.	Sex and Age.	Condition of liver.	Operation.	Result.		Ascites.	Remarks.
						Immediate.	Ultimate.		
1	1889	Van der Meule	.....	Cirrhotic (?)	Omentum stitched in wound (?)	Death from shock.			
2	1891	Schekly.	M.	Cirrhotic.	Omentum stitched in wound (?)	Death 14 days.	.....	.....	During delirium patient tore off dressings, and infected wound. Death from peritonitis.
3	1892	Thomas Lens.	M. 61	Atrophic cirrhosis.	Omentum stitched in wound.	Recovery.	Death 6 mos.	Unimproved.	Failure attributed to atrophic condition of the liver.
4	Sept., 1894	R. Morison (Drummond).	F. 42	Large, pale, smooth (not cirrhotic).	Liver, spleen, omentum, and parietal peritoneum sponged; drainage.	"	Death 19 mos.	Unimproved.	Frequent tapping required. Diagnosis of cirrhosis not confirmed.
5	Oct., 1895	R. Morison (Drummond).	F. 39	Typical cirrhosis.	Liver, spleen, omentum, and parietal peritoneum sponged; drainage.	"	Recovery.	No recur- rence.	Well two years later. Death due then to operation for ventral hernia.
6	March, 1896	Von Eiselesberg and Narath (Talma).	M. 9	Enlarged, surface granular; spleen enlarged.	Gall-bladder and omentum stitched to abdominal wall; no drainage.	"	"	Trace.	Three operations. Two years after seemed perfectly well. Spleen much smaller; liver still hard but functions good. No ascites.
7	Jan., 1897	R. Morison.	M. 42	Small, lobulated; spleen six times normal size.	Liver, spleen, omentum, and intestinal coils sponged; drainage.	"	"	No recur- rence.	Depression and excitement followed operation. Well two years after, and no return of ascites.
8	March, 1897	R. Morison.	F. 54	Advanced cirrhosis; spleen enlarged.	Omentum sutured; no sponging.	Death 11 days.	.....	.....	Complications, large interligamentary ovarian cyst and umbilical hernia. Cirrhotic kidneys. Death due to uremia.
9	Oct., 1898	Narath (Talma).	M. 59	Hard, nodular, capsule thick; spleen enlarged.	Omentum and parietal peritoneum sponged and stitched together.	Recovery.	Recovery.	No recur- rence	Melancholy before operation; after, delirium and melancholy. Improved by reduction in nitrogenous foods. Eventually recovered entirely.
10	Nov., 1898	R. F. Weir.	M. 39	Cirrhotic, nodular, and fatty.	Liver scraped with bat- tin; omentum stitched to abdominal wall; drainage.	Death 5 days.	.....	.....	Septic peritonitis from drainage-tube. Echinococcus cyst of liver.





If we eliminate the first three cases because the operative procedure at that time seems faulty and the technique not as perfect as it is to-day, and also the fourth case because the diagnosis of cirrhosis is doubtful, we have a total of eighteen cases, with three immediate deaths (one from infection and two as the result of kidney complications), one ultimate death, three unimproved, two improved, and nine recoveries.

Placed in percentages it will read :

Immediate death . . . . .	16.6 per cent.
Ultimate death . . . . .	5.5 "
Unimproved . . . . .	16.6 "
Improved . . . . .	11.1 "
Recovered . . . . .	50.0 "

If we still further eliminate No. 8 because the operation was complicated by the removal of a large interligamentary ovarian cyst and the radical cure of an umbilical hernia, and No. 10 on account of the presence of a hydatid cyst of the liver, and also Nos. 13 and 14 because the cirrhosis of the liver was not primary, but secondary to a chronic peritonitis, we will have a total of fourteen cases, with one immediate and one ultimate death, one unimproved, two improved, and nine recoveries. In the table of percentages it will read :

Immediate death . . . . .	7.1 per cent.
Ultimate death . . . . .	7.1 "
Unimproved . . . . .	7.1 "
Improved . . . . .	14.3 "
Recovered . . . . .	64.3 "

Contrasting the worst view with the best possible construction we can place on this table, we have the operative mortality lying somewhere between 23 per cent. and 7 per cent. and the recoveries between 41 per cent. and 64 per cent. When we remember that the cases subjected to operation had been for weeks or months under careful medical treatment and had been repeatedly tapped, and that their condition was unimproved or growing steadily worse, the above statistics are certainly very encouraging. Weir has aptly said : " Of necessity, in the early stages of any surgical measure such as this, one must and should operate only on those patients who are regarded

as hopeless of cure by any other means." This, of course, reduces the chances of success to a minimum.

It is interesting to note that in one case (No. 12) operation was undertaken on account of severe hemorrhages from the bowel. The patient had hypertrophic cirrhosis without ascites, and after operation the hemorrhages ceased. Talma in this connection recommends that where hemorrhages from the œsophageal plexuses are free, operation should be performed.

In speaking of the chances of success or failure after operation Talma lays particular stress upon two points: 1. That the cirrhosis of the liver is a primary one, and not secondary to some other disease, as chronic peritonitis with serous effusion. How such a differential diagnosis may be made before operation we do not know, but the points of difference when the peritoneum is once opened are marked. In a primary cirrhosis the thin and glistening character of the peritoneum is scarcely altered from the normal, although many fine injected bloodvessels may be seen through it, while in chronic peritonitis the membrane is tough, much thickened, and has lost its glistening character. 2. That the function of the liver cells must still be good. If the liver is so atrophied that the functions of its cells are reduced to their lowest ebb it is not to be presumed that operation will restore such function or prolong life, although the ascites may not return.

Let us look for a moment at some of the opinions expressed by others. Rolleston and Turner advise early operation, before the liver tissue becomes so degenerated as to be beyond the hope of undergoing any improvement. They believe that medical treatment should be persisted in only while the diagnosis is in doubt, and should be especially directed to counteract any possible syphilitic disease of the liver. When a course of iodide of potassium has not benefited a case of ascites which is thought to be due to either syphilis or cirrhosis, medical treatment should be suspended and operative measures employed. They further recommend that when cirrhosis can be diagnosed with fair certainty in the preascitic stage, from the presence of hæmatemesis, enlarged spleen, etc., operative treatment would probably succeed better than in the later stages. Morison believes that it is no longer advisable to treat ascites due to cirrhosis

of the liver by repeated tapplings if the patient is otherwise sound and in fair general condition. After one or two tapplings have failed operation offers the best chance for a prolonged and useful life. Talma's views are practically the same. Friedmann states that a *sine qua non* before operation is undertaken is that the liver cells must still have the power to act—*i. e.*, before the liver is too far degenerated—and recommends operation not later than after the second tapping.

Expressions such as these by men who have given the subject much thought and careful study, and who have had a personal experience with the operation, are not to be brushed aside lightly.

CONCLUSIONS. *A priori* cases of cirrhosis of the liver stand injury badly, and therefore are poor subjects for operation. The resistance of their tissues is presumably much less than in health. The exact estimation of the amount of degeneration of the various organs, including the liver, is extremely difficult or impossible, consequently the mortality of the operation under consideration would naturally be expected to be relatively high. The statistics given above seem to show that the operation has won a distinct place, and in the future a clearer conception of the suitability of particular cases for the operation may be possible. Without operation these patients as a class are doomed to a life of perpetual invalidism, requiring constant treatment and repeated tapplings to make life bearable. It is our opinion that where the diagnosis of pure portal cirrhosis of the liver can be made, and where persistent and well-directed medical treatment is productive of insignificant results, the operation should be strongly recommended. On the other hand, it would seem that the operation is scarcely indicated, if not contraindicated, in cases of ascites associated with other kinds of cirrhosis (Hanot's, syphilitic, mixed, etc.), or with chronic peritonitis.

NOTE.—In an abstract in the *Lit. Beilage der deutsch. med. Woch.*, January 3, 1901, p. 7, reference is made to an article by P. Commandini and W. Salvolini (*Gaz. degli Ospedali e del. Clinic.*, No. 150), in which two cases of cirrhosis of the liver are reported where the omentum was sutured to the abdominal wall. In one death occurred on the fourteenth day after operation, in the other

the ascites quickly returned. The reference was seen too late for incorporation into our table.

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## DISCUSSION.

DR. CHARLES BAUM: I recently saw a case of cirrhosis of the liver in which Dr. John B. Deaver made an abdominal incision, and six months afterward there had been no return of the ascites. I have not seen the patient for four months. The patient was a drinking woman, between forty-five and forty-six years of age. She had not had a return of the ascitic fluid.

Another case came under my observation some time ago in which I tapped a woman forty-eight times. By measurement five hundred and twelve ounces of fluid were withdrawn at one time, some fluid having been lost. She had two attacks of severe hæmatemesis. For some time tapplings were necessitated every two weeks, and finally she died at sixty-two years of age. The duration of the disease was three years. There was no history of alcohol or syphilis. One other feature I would mention, when medical means apparently had failed: she took as many as four drops of croton oil without any effect. One week later, by accident, she was given a spoonful of Husband's magnesia, which gave her three profuse liquid stools. Until her death, from exhaustion, this medicine would cause a liquid stool.

DR. JAMES TYSON: I have had one case of cirrhosis of the liver, operated for ascites. The history is as follows: The patient was under my care in the Philadelphia Hospital in April, 1900. He was tapped while there and

treated with diuretics and aperients until finally the fluid ceased to return, and he was discharged apparently cured. A month or two later he was admitted to my wards in the University Hospital with a large accumulation of fluid, where he was again tapped a number of times. His health was evidently failing, when I left for my holiday, and he passed over to the surgical wards of Dr. Frazier, and during the summer he was operated on. I found him again in my wards on my return apparently relieved by the operation. He remained under observation until Christmas, when he was discharged. Naturally the impression I gain from the experience of the operation is a favorable one. I trust that Dr. Frazier is here and can say something more about the operation himself.

DR. JOHN B. DEEVER: I would like to go on record as having had one operation of the kind reported; the patient died. I have seen permanent recovery follow simple tapping.

I very much question if it promises as much as we think. I believe cirrhosis of the liver is only part and parcel of a general cirrhotic process, and the liver being a huge organ, we have more pronounced evidence of the cirrhotic process here than elsewhere. I would, therefore, trust to tapping rather than having the abdomen opened up with the idea of exciting the formation of adhesions, etc.

DR. ARTHUR V. MEIGS: One of these patients was under my care, having been transferred to me on December 1st, when I went on duty at the Pennsylvania Hospital. He died five days after I took charge of him. Dr. Le Conte quotes one authority as recommending immediate operation in cases of cirrhosis of the liver pure and simple, in which the patient is in other respects well. It has not been my good fortune to meet with such cases. People I have dealt with having cirrhosis of the liver have always had grave diseases of other organs, and it seems to me, for this reason, that the operation can have only a limited use. It is like the operations which have been done for the relief of aneurism of the great vessels within the thorax, they have been very unsuccessful, because the patients are always greatly diseased in other ways.

I should like to ask Drs. Le Conte and Packard in regard to one point. I was present at the autopsy, although I did not make it myself, and it was already established that the operation had been successful in causing the formation of adhesions. Do they believe it is established that a collateral circulation was formed? I have examined such adhesions with the microscope, and it seems to me that as a general thing they are nearly avascular. They are generally fibroid and poorly supplied with bloodvessels. I should like to ask whether the formation of the adhesions proves that a collateral circulation also had been established.

DR. D. L. EDSELL: I should like to ask whether in the cases reported by Drs. Le Conte and Packard, or in any other cases which they have found recorded, there have been any studies of the occurrence of glycosuria,

alimentary glycosuria, or actual diabetes after the operation. The relation of the liver itself to diabetes is, of course, obscure, but the most satisfactory experimental evidence, and I think clinical evidence also, indicates that the liver has no direct relation to diabetes; but the chief reason that I ask the question is that the direct introduction of sugar solutions into a vein, or the absorption of sugar into the lower hemorrhoidal veins which empty into the cava and not into the portal system will produce an "alimentary" glycosuria. In the operation described a large part of the portal circulation is switched off into the general venous circulation, hence the sugar absorbed along the whole gastro-intestinal tract is to a considerable extent passing directly into the general venous circulation, and I should think there would likely be glycosuria, particularly after the administration of a considerable quantity of grape sugar solution—that is, so-called alimentary glycosuria. From a consideration of animal experimentation, it does not seem probable that the operation under discussion would produce diabetes, simply because the liver is to a considerable extent excluded from the portal circulation. One other factor, however, makes diabetes seem a not impossible result—that is, that in these cases there is usually a considerable degree of general arterio-sclerosis, and arterio-sclerosis seems to have a fairly close relation to a considerable number of cases of diabetes, particularly of mild form. It seems possible that the alteration in the circulation, combined with the arterio-sclerosis, could cause the symptoms of diabetes, though in the instances of this operation which I have seen reported no such symptoms were recorded. Should it occur it would, of course, influence one in deciding upon the operation, and would also influence the prognosis.

DR. LE CONTE: In the cases that Dr. Packard and I were able to collect—twenty-two in number—there was no mention of glycosuria being present, so we infer that it did not occur. In some of the experimental work done upon dogs, particularly by Hahn, Massen, etc., there is a discussion on this point, and if I remember rightly some of the dogs showed sugar in the urine. In answer to Dr. Meigs' question, whether the collateral circulation was established in the case which lived sixty-one days, I would say yes. The adhesions were examined microscopically and numerous blood-vessels were found in them. Adhesions, unless injected, will scarcely show blood at the time of the post-mortem examination, as the vessels are then empty. Again, from the fact that the man had no demonstrable ascites from the time of operation until he died, and that previous to the operation he had to be tapped every few days, I should say that a collateral circulation had been of benefit. The pictures which we show illustrate well the large size of the abdominal veins. These veins were present only in a very slight degree before the operation, and since then have slowly increased in size. I therefore judge the operative results have been good so far as the collateral circulation is concerned.



EXHIBIT OF WAX MODELS OF CUTANEOUS  
DISEASES, WITH REMARKS UPON THE  
USES OF WAX MODELS AND THEIR  
PREPARATION.

By JAY F. SCHAMBERG, M.D.,

AND

J. FRANK WALLIS, M.D.

[Read February 6, 1901.]

THOSE of you who have visited the large medical museums of Europe must have been much impressed with the extensive array of beautiful wax models there on exhibition. One of the finest of these collections is in the St. Louis Hospital, at Paris, in a museum devoted to the representation of cutaneous diseases. The artists who made these models and those who commissioned them have always maintained considerable secrecy concerning the process of their preparation. While abroad some years ago I made sundry unsuccessful attempts to obtain some knowledge upon the subject. I am indebted for my information to Dr. William S. Gottheil, of New York City, who read an article on "Plastic Models and their Uses" before the New York County Medical Society in 1893. During the past few months Dr. Wallis and myself have devoted some time to the preparation of wax models, which we have the pleasure of exhibiting to you this evening. These models were made directly from patients presenting themselves at the skin department of the Polyclinic Hospital.

No. 1 represents a gummatus syphiloderm of the leg, showing ulcers upon the foot and leg, with a large gumma upon the ankle just about to break down. These lesions have appeared three years after an innocent chancre of the gum in an untreated young woman.



No. 2 is a case of supra-orbital herpes zoster in a colored woman. The unilateral character of the eruption is here well shown.

No. 3 shows an epithelioma of the face of a woman, aged eighty-three years. The model was made while the patient was undergoing destructive treatment of the growth with caustic potash.

No. 4 represents a beginning psoriasis upon the breast of a young girl.

No. 5 shows the breast of a woman with carcinoma. The nipple is seen to be retracted, but in addition to this there is a very unusual condition in the overlying skin. There are here seen, surrounding the nipple in a radiating manner, numerous enlarged bloodvessels and lymphatics.

No. 6 is an excellent example of an ulcerative crustaceous syphiloderm, showing here and there ulceration of the patches where the crusts have been removed.

No. 7 represents a papulo-pustular acne of the face in a young girl.

No. 8 represents a herpes zoster involving the scapulo-humeral regions.

No. 9 represents a nodular epithelioma of the back of the hand of six months' duration.

No. 10 represents a case of psoriasis, showing typical patches covered with silvery scales upon the flexor surface of the forearm.

No. 11 represents a highly inflammatory erythematous-squamous eczema of the back of the hand in a market-woman.

No. 12 represents an acute erythematous eczema of the eyelids and face in a middle-aged man.

No. 13 represents exfoliation of the nails of the hand in a case of acute exfoliative dermatitis, probably resulting from the administration of large doses of antipyrine.

No. 14, a series of models representing the evolution of the vaccination lesion upon the fourth, sixth, ninth, twelfth, and fourteenth days; also a spurious raspberry-mark.

No. 15, a model representing the arm of a mulatto, covered with a discrete but well-marked eruption of smallpox. The lesions are fully developed pustules, representing the seventh day of the eruption. (Casts made at the Municipal Hospital through the courtesy of Dr. Welch.)

The trend of medical teaching to-day is in the direction of the elimination to as great a degree as possible of didactic instruction and its substitution by clinical teaching. It is impossible, however, for the lecturer in medicine to have constantly at his command appropriate material to illustrate the lectures which he happens to have reached in his systematized scheme of teaching. It is at such times that photographs—particularly projected photographs—drawings, paintings, and wax models are of distinct value. These reproductions serve not only as substitutes for clinical teach-

ing, but they may be used for the faithful preservation of visual changes observed in rare cases of diseases.

Wax models have manifold advantages over pictorial representations in the flat. The artist is obliged to represent prominences and depressions—in other words form—by light and shadows. No matter how skilfully this is executed it is apt to modify or even distort normal color values and effects. It is difficult, also, to have the artist view the changes to be portrayed as the physician does. The making of the wax model itself is purely mechanical, and the personal equation of the artist does not affect it. Its coloring, being a simple copying from nature, is not so susceptible to artistic distortions.

The ingenious advances made in color photography by Mr. Ives, of this city, will doubtless enable projected color photographs to be used in didactic medical teaching. There are, however, certain obstacles still in the way of its free employment, notably the long exposure required to make the plates.

The first step in the making of a wax model is the preparation of the mould or cast. This is made of plaster-of-Paris, of which the variety used by dentists is the best. The skin is to be prepared for the reception of the plaster by painting it with olive oil. Wherever hair is present, as upon the eyebrows and moustache, it must be carefully anointed with a stiff ointment, such as resin cerate. The imprisonment of the hair in the plaster is a most painful and embarrassing accident. If the eyelashes are well greased with vaseline they give no trouble, as a rule. The eyelids should be kept well shut, in order to keep out the irritating particles of plaster. It is necessary to limit the spread of the plaster in applying it to the skin. This is best accomplished by laying wet towels about the proposed boundaries of the parts. The plaster is sprinkled in handfuls or through a sieve into a basin of water until the latter absorbs no more plaster. After the plaster is entirely submerged, and not until then, the mass is stirred. The stirring should be carefully continued until the plaster acquires a creamy consistence. It is then rapidly poured upon the skin, care being taken to bring it in contact with the entire surface while yet fluid, in order that it may insinuate itself into all of the depres-

sions of the skin. It is then built up to a desirable degree of thickness and allowed to set. The setting is indicated by the development of warmth. This ordinarily takes from five to eight or ten minutes, depending upon the consistence of the original plaster mass and the temperature of the water. The cast is then removed.

All of the models presented here this evening have been made from moulds cast in a single piece. If it is desired to make a cast of the whole circumference of a part such as the arm, or of a region where there are undercuts, it is necessary to make the cast into two or more sections. This is done by laying a well-oiled thread over the most prominent aspect of the part and pulling it through the plaster before the latter has become hard.

After the mould has been completed the wax may be immediately poured into it or it may be set aside until any convenient time. If the cast is allowed to become dry it must be soaked in water for a half-hour or more before the wax is poured in, otherwise the model will be spoiled by the development of air-bubbles.

Before pouring it is desirable to build a wall of plaster about the edge of the cast in order to give it a basin shape, so that it will hold a considerable amount of the molten wax. The wax composition employed is as follows :

White wax	. . . . .	1 part.
Yellow wax	. . . . .	2 parts.
Paraffin (about 54° C. melting-point)	. . . . .	1 part.
Starch	. . . . .	2 parts.
Talcum	. . . . .	3 "

The wax and paraffin are melted together upon a water-bath in an ordinary double boiler, and the starch and talcum, previously mixed, are thoroughly stirred into the mass. More or less of a flesh-tint may be given to wax by incorporating carmine in it. Either a small quantity of powdered carmine may be rubbed up with the starch and talcum, or it may be dissolved in alcohol and the necessary quantity poured in and stirred. The wax is now poured into the mould up to the brim and then poured back again into the receptacle. It is important in this first pouring to bring the wax rapidly into contact with the entire surface of the mould,

otherwise indelible furrows will be produced in the resulting models. The pourings are now repeated until the model has acquired a sufficient thickness (ordinarily from one-eighth to one-quarter of an inch). It is then allowed to cool, after which the plaster cast is broken piecemeal from the model. Where there are no undercuts the model may often be removed from the cast without destroying the latter. To accomplish this the model must be removed before it is quite hard, while it still has some elasticity.

Most models require some obliteration of imperfections and smoothing down of the surface by the use of graving tools, and, if necessary, by rubbing with benzine.

Powdered colors, water-colors, and oil-colors may be used to properly portray surface tints. Powdered colors are not permanent and may show implantation of visible granules. Water-colors have the advantage of transparency and are particularly useful in applying the skin-tint. In order to employ water-colors a menstruum must be used which is capable of mixing both with water and wax. Such a preparation is "turkey-red oil"—a substance occurring as a by-product in the manufacture of alizarin. Dr. Wallis and I have made exclusive use of oil-colors in these models, using, to be sure, very little paint in the applying of the flesh-tints. Oil-colors are the most permanent of the various pigments, and may be blended with greater facility.

While wax models lend themselves admirably to the portrayal of cutaneous diseases, they need by no means be restricted to this use. They may be employed wherever there are visual changes upon the surface of the body, whether they represent integumentary diseases or deviations from the normal musculature or ossature.

They may, therefore, be employed by the general surgeon to reproduce the appearances of tumors of all kinds visible upon the surface, and of deformities occasioned by rare fractures and dislocations, etc. The orthopedic surgeon may portray with them the various forms of club-foot, congenital malformations, and all of the other deformities which come within his province. The medical clinician will find them useful in the reproduction of the

appearances of acromegaly, myxœdema, muscular atrophies and hypertrophies, arthropathies, joint changes such as are seen in gout and rheumatoid arthritis, etc.; and, finally, the pathologist will find them invaluable in perpetuating the appearances of organs and tissues as seen at autopsies. Physicians and students would doubtless evince more interest in and derive more instruction from a collection of well-executed wax models of pathological specimens than from the rows of jars containing shrunken and decolorized specimens so frequently encountered.

The making and coloring of wax models requires no great amount of artistic genius, but merely some technical knowledge of colors and a little aptitude for the work. The materials are inexpensive and the consumption of time not as great as one would be inclined to think.

## DISCUSSION.

DR. JAMES K. YOUNG: I would like to ask Dr. Schamberg how he protects the nose in making the casts in order that the patient may maintain respiration?

DR. SCHAMBERG: In response to the query of Dr. Young, I would say that in making a cast of the face it is necessary to leave open an avenue of respiration, and this is done by the insertion into the nostrils of quills, or, preferably, rubber tubing. Care must be exercised not to close up the apertures of these tubes. A member of the College has informed me that while taking instruction in the making of casts some years ago in Vienna, and applying the plaster to the face of the daughter of the expert, he accidentally cut off all channels of breathing. The father, in order to prevent his daughter from suffocating, was obliged to break the cast with a hammer. I have never had any accident of this character, and, indeed, with ordinary caution there is little or no danger.

## NOTES ON FIFTY OPERATIONS FOR OTITIC EXTRADURAL ABSCESS.

By ALEX. RANDALL, M.A., M.D.,

CLINICAL PROFESSOR OF DISEASES OF THE EAR IN THE UNIVERSITY OF PENNSYLVANIA, ETC.

[Read February 6, 1901.]

WHILE long clinically known to the general surgeon as results of trauma, extradural abscesses, as well as those of the cerebrum and cerebellum, had not received their due recognition until the advances of localization and intervention made operations in this field more justifiable and fearless. Since then the post-mortem teachings have been more than borne out by the clinical experience as to the frequency of the aural causation of such lesions, and the otologist has been doing his full share in advancing as well as forestalling this notably successful branch of surgery. This is the more the case as to extradural collections of pus, for the reason that they are so frequently devoid of other than aural symptoms, and in major as well as in minor forms are unexpectedly found in interventions which were not planned to enter the cranial cavity. Until recently the surgeon, general or special, inclined to undue caution in the matter of uncovering the dura mater. This was most judicious when asepsis in such work was not thorough, and still befits those who employ (as two recent surgical treatises by prominent authors advise) a gimlet or other boring tool for opening the mastoid. Needless to enter the cranial cavity, especially by bungling operation, is certainly to be deprecated; but modern experiences in such work show that the safety and promptness of success are much enhanced by following to the end every unhealthy track in the bone, whether actually

carious or only presumably infected and no longer viable. Thus only can we fairly count upon eliminating the beginnings of serious trouble. Without this, the more solid the superficial healing which we secure the more dangerous do we make the lesions lurking in the deeper tissues.

No aural surgeon of wide experience is able to retain his callow trust in the efficacy of the Wilde incision—a mere periosteal section over the inflamed mastoid. External mastoid periostitis may primarily occur, perhaps, but the best authorities are skeptical even as to the cases of their own which they had so diagnosticated in the past: while most of the publications of such cases give clear internal evidence of erroneous diagnosis. We know by huge series of cases (I have personally had upward of a thousand) that all of the signs of severe inflammation of the mastoid—pain, tenderness, redness and a swelling that thrusts the auricle almost straight out from the head, due to œdema that could hardly be distinguished from fluctuation—all this has passed away in a few days under mere rest in bed. Heat or cold to the aural region, hot douching in the canal, leeching or other antiphlogistic measures may have aided the resolution, and any one of these may have received undue credit for the result. Especially is this so in my opinion as to the incision or counter-irritation over the mastoid—any case that can be brought to resolution with these measures would have done as well or better without them.

It is very different when pus is present on or in the mastoid. Resolution and absorption are perhaps conceivable, but the surgeon who waits for them is tempting Providence. There is far less danger in operation than in delay. Exit may occur spontaneously or under mere incision of the soft parts: and the carious or infected bone may crumble and exfoliate in the course of weeks, months, or years as completely and safely as it could be removed by the surgeon in a few minutes: but the probabilities are strongly against any such equality. No life insurance company can usually be induced to accept as a proper risk a person with aural caries: and the presumption is strong that there will at least be an extension of the infective and destructive process beyond the limits to which it might have been confined by prompt surgical effort to eradicate the focus. Pus



upon the surface of the mastoid has rarely formed there. It may have burrowed out subperiosteally along the canal or have seeped through the apparently healthy cortex. Its exit through a large bone sinus may be so frank as to tempt us to believe that drainage is already adequate without operative attack upon the bone. Any considerable experience will show this to be fallacious. The healthiest-looking bone may wall in a pus-collection which is not merely menacing local structures and tending to general pyæmic infection, but is burrowing between the dura and the skull and locally infecting the intracranial contents. How often this is the case is only growing into recognition. In my first hundred mastoid operations there were not many in which I recognized the need to lay bare the dura: but there were too many in which I had later to do by a second operation what had thus been left undone. In my second hundred operations I found the disease to have involved the inner table in greater or less degree in nearly one-half of the cases, and in the still more thorough and less timid work of my third hundred operations these extensions have been actually in the majority. What my further experience may show is hardly more than foreshadowed, as my fourth hundred is not half-completed: but some of my most notable instances of dural involvement have fallen in this period. Laying aside the small penetrations where the inner table was carious, but the dura not notably involved or lifted by distinct pus-collection, there have been fifty cases to which the title of extradural abscess must be fully conceded, so notable was the granulating pachymeningitis or the interposed pus-collection: and it is of some of their teachings that I now wish to speak.

A few instances will illustrate some of the varieties of the conditions and the difficulties of diagnosis previous to intervention: although without very tangible symptoms one may often hazard a close guess as to what will be found. It is only fair to remark that many of the cases have been operated on within an hour or two of their coming to me, so that I have made no delay in the interest of a diagnosis more precise than that intervention was demanded. So likewise I have not often by procrastination given opportunity for the interoccurrence of complications. To me it is remarkable the usual absence of symptoms suggesting intracranial mischief in even the



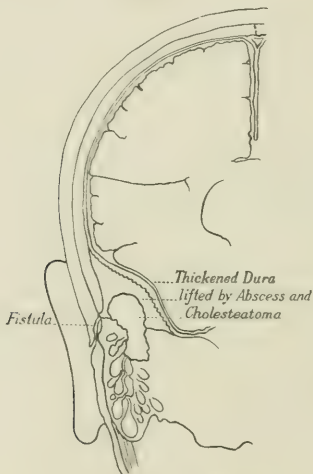
worst cases. The subnormal temperature or slowed pulse commonly indicative of cerebral abscess was lacking wholly, although the bulk of the intracranial collection often was enough to presuppose decided pressure. The extent of the dura covered with villous granulations was at times markedly at variance with nearly normal temperature and apparent well-being. The eye-grounds were almost invariably studied, and in but one or two instances showed any suggestion of involvement; the hearing was usually good except as explained by peripheral conditions, and paretic or inco-ordinate symptoms were absent. The uneventful and generally prompt progress of the cases to lasting cure was a delightful contrast to the results imminent in some of them and of known deadly outcome in some not operated on.

CASE I. *Acute grippl tympanic suppuration with mastoid empyema breaking into the digastric fossa; perisinus abscess and rupture of sigmoid sinus; recovery.*—A man, aged sixty years, had intermittent pain and febrile condition, with tenderness of the left mastoid unrelieved by early and free opening of the drum-head. After three weeks, exacerbation with prominence of the sternomastoid, pressure on which filled the canal with pus. Operation showed a thick mastoid cortex within which the whole mastoid was one cavity with pus and necrotic granulations. A cautious use of the probe was followed by a gush of venous blood, instantly controlled by the finger. Gauze was packed down and back upon the sinus, while the mastoid was more freely opened and curetted clean; then on carefully unpacking the sigmoid was seen bared for an inch and its wall covered with granulations. The carious edges of the inner table were freely removed, and, after the mastoid tip and the digastric collection had been fully dealt with, the sinus wall was gently curetted without recurrence of bleeding. Healing was rapid and smooth.

CASE II. *Chronic tympanic suppuration with recurrent fistula on mastoid; cholesteatoma breaking through tegmen; large extradural abscess of middle fossa draining through the squama; recovery.*—A man, aged fifty-six years, came (October 10, 1899) with a recent fistula high on the mastoid, where more than a year before apparent healing had followed evacuation of pus by incision of the soft parts. There were pain and much tenderness, with slight swelling about the ear; twitching of the left side of the face had been long present and was perhaps now exaggerated; the canal was full of crusts and pus coming from a small upper perforation. Little probing of the fistula was tolerated, but rough bone could be felt up and forward, and the surmise was hazarded that there was an outbreak through the squama of extradural pus. On operation a 10-millimetre opening was found above the supramastoid crest with a cholesteatoma mass presenting within it

(Fig. 1). Pus escaped to the amount of nearly two ounces as this was pressed aside in enlarging the opening, and the cholesteatoma was found largely embedded in the roofless tympanum. There was little mastoid caries below the antrum, which was well curetted with care not to injure the facial canal; but in scraping the edges of the tegmen I feared that I had reached the hiatus Fallopii, and ascribed the facial palsy, which immediately appeared, to my intracranial work injuring the geniculate ganglion. Healing was good, though slow.

FIG. 1.

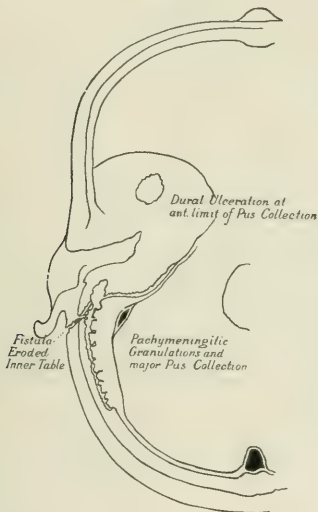


(Case 2)  
Fig 1

CASES III. and IV. *Persistent mastoid fistula after repeated rigorous operation; extensive pachymeningitis externa with ulceration through dura; recovery.*—One week last October brought these and the following case: Each of these was a boy, aged about ten years, with a small postaural fistula left after one or more operations by good surgeons. Probing revealed bare bone to a considerable depth, and operation opened up extradural suppuration over the tegmen extending forward almost to the sphenoid and with the dura ulcerated (Fig. 2) through at the anterior part of the middle fossa, so that the brain prolapsed in front of the down-turned spoon with which

I was curetting the bony floor. In one case the dura, down and inward, was lifted almost to the *foramen magnum*; and there had been posteriorly a patch two inches square of pachymeningitic granulations so luxuriant in their growth as to resemble the brain convolutions as they were first brought to view. Recovery was not complete in one case until thirteen weeks, and the other has been a little slower.

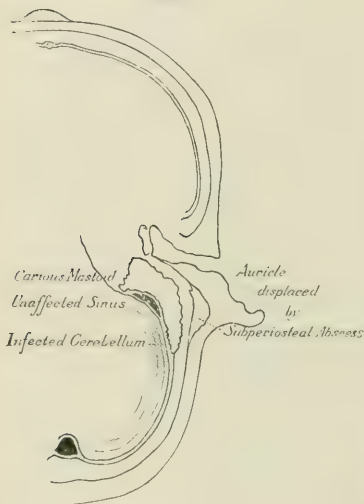
FIG. 2.



*CASE V. Acute empyema of mastoid with destruction of its entire inner table; dura discolored and cerebellum softened; fungus cerebelli; recovery hardly yet complete.*—A girl, aged fifteen years, showed mastoid swelling and a tenderness that precluded positive recognition of fluctuation before ether. There were two drachms of pus on the mastoid, but the bone looked normal except that the sutural lines were blackish. The outer table was 5 millimetres thick, and the entire mastoid within was converted into one cavity from which thick, foul pus pumped out under the pressure of the brain pulsations. The whole inner table was gone and the dura was rough and discolored. After thorough curetting of the antrum and scraping clean the

mastoid interior, the field was flushed with sublimate, and the most unhealthy-looking area of the dura was incised where its bulging resembled the knee of the sigmoid sinus. Puriform yellow material was found and was curetted away in the line of the sinus, but no inner wall could be felt, and normal-looking cerebellar tissue was reached in all directions. Examination of this creamy detritus showed multipolar cells and teeming staphylococci (Fig. 3). The sinus was anterior to the softened cerebellar

FIG. 3.



(Case 5)  
Fig. III

FIG. 4.

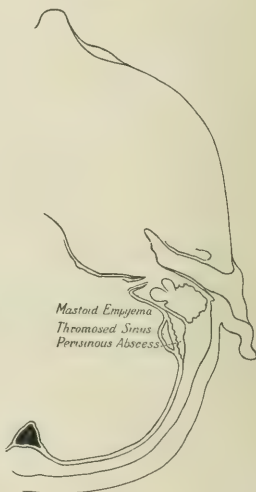


Fig. IV.

area and not recognizably thrombosed, so in the absence of high temperature its firm wall was not incised. There was oedema extending to the brow and closing the right eye, but none below or behind the mastoid. Cerebellar hernia formed, but had healed, when she was allowed to go to work; and slight protrusion had recurred when last seen before she ceased attendance.

Time permits but a few concluding remarks. I hope I have made it clear to others, as it certainly is to myself, that in acute as in

chronic cases very extensive intracranial penetration of pus can be present with minimum symptoms ; and this not only in those patients with an extra thick mastoid cortex, which hinders ready breaking outward of the empyema, but in some in whom the yielding of this part of the bone has been exceptionally quick. Free incision of the soft parts may be reserved for the cases with fluctuation ; but should then be employed as a step to the duly thorough exploration of the bony structures, without which the surgeon leaves himself in needless darkness as to the real condition and dangers of his patient. The antrum should be freely opened in the acute cases—*all* of the tympanic cavities in the chronic—not only for drainage but for full inspection of the walls ; and every portion of diseased or decidedly suspicious bone curetted away. If this lead the operator through the inner table to the dura, instead of shrinking from such intervention, he should rather thankfully follow the clue, glad that no apparently healthy wall hides from him the deeper lesion and deceives him into deferring to a second and perhaps too tardy intervention the relief which it is his duty to afford. Extradural abscess well evacuated is wonderfully harmless ; but it is the cause or the method of propagation of many of the most serious or fatal of the intracranial extensions of tympanic suppuration.

# A SKIAGRAPH OF BENNETT'S FRACTURE OF THE METACARPAL BONE OF THE THUMB OR "STAVE OF THE THUMB."

By JOHN B. ROBERTS, M.D.

[Read February 6, 1901.]

THROUGH the courtesy of Dr. George Thomas Beatson, of Glasgow, Scotland, I am able to show a Röntgen-ray print of this fracture. The injury was accurately described in 1885 by Professor E. H. Bennett, of Dublin, Ireland, but has not attracted as much attention in this country as it should.

The fracture occurs obliquely at the base of the metacarpal bone of the thumb on its palmar aspect detaching a portion of the base of the bone. It runs into the joint between the metacarpal bone and the trapezium. As a result of this detachment of a considerable portion of the articular surface, the metacarpal bone is displaced backward and gives a deformity similar to that of a posterior subluxation. The injury is usually caused by a blow applied in the long axis of the thumb. The pain causes a disability in apposing the thumb to the index finger and probably to the other fingers. Grasping small objects becomes impossible and pressure on the ball of the thumb gives pain. The injury is likely to be mistaken for subluxation, sprain, or contusion. It is to be treated by extension and full abduction of the thumb, which posture should be maintained by a gypsum or other splint. The skiagraphs of Dr. Beatson's case were taken sixteen days after the injury and at the conclusion of treatment. The fracture, until seen by Dr. Beatson, had been unrecognized and had not been reduced.

The attention of the Fellows is called to this injury because it is probable that it is usually overlooked. I have never recognized the fracture, though the inspection of the skiagraphs calls to my mind an injury of the thumb, seen some time ago, which was not clear to me. It is possible that it was a case of this kind.

FIG. 1.





FIG. 2.



FIG. 3.

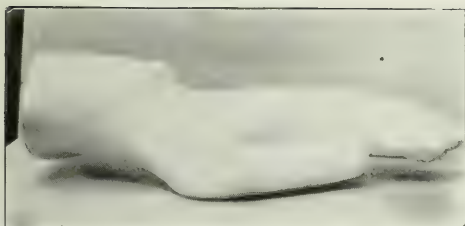


Fig. 4.



## A CAST AND SKIAGRAPH OF THE SO-CALLED SMITH'S FRACTURE OF THE LOWER END OF THE RADIUS.

BY JOHN B. ROBERTS, M.D.

[Read February 6, 1901.]

SEVERAL years ago I showed a series of specimens from the Mütter Museum illustrating fracture of the lower end of the radius, with anterior displacement. There were shown at that time skiagraphs of fractures of this sort. In a monograph presented to the American Surgical Association in 1896, I recorded a number of instances occurring in my own practice and collected from various sources. Experience in and study of this injury have convinced me that it is frequently overlooked. Of the five or six cases which I have seen there was probably not one in which the character of the injury was clearly understood by the practitioner who first saw it.

It is a great pleasure to be able to present to the College a cast and a skiagraph of an old injury of this sort, sent me by Dr. George Thomas Beatson, of Glasgow, Scotland. The case was one which Dr. Beatson did not see until a year after the accident. It occurred in a woman, aged forty-six years, who fell from a bicycle. The deformity corresponds with that usually seen, and the skiagraph is almost a perfect reproduction of the specimen in the museum of the New York Hospital, a picture of which was given in the article to which reference has been made. It is unnecessary to speak of the treatment in full at this time. It may, however, be said that it requires the application of force, often great force, to break up the impaction and restore the fragments to their normal relations. A moulded splint, made of metal, gutta-percha, or gauze and plaster-of-Paris, should then be applied to the palmar surface. In some cases a straight splint may be applied to the dorsal surface instead of the moulded splint to the palmar surface.

# PERFORATING ULCER OF THE STOMACH; OPERATION; RECOVERY.

By JOHN H. MUSSER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, UNIVERSITY OF PENNSYLVANIA.

AND

HENRY R. WHARTON, M.D.,

CLINICAL PROFESSOR OF SURGERY IN THE WOMAN'S MEDICAL COLLEGE; SURGEON  
TO THE PRESBYTERIAN AND THE CHILDREN'S HOSPITALS.

[Read February 6, 1901.]

G. C., aged forty years, single; farmer; resident of Maryland. He used tobacco moderately, but no alcohol. He was regular in his meals, and his dietary was not an unusual one. He had had much care and anxiety.

Had dyspepsia for many years previous to present attack, chiefly of acid form. For three months prior to the date of the symptoms for which he required operation he suffered from pain in the epigastrium and occasional attacks of vomiting. He never vomited blood. The pain was often relieved by food, so that it was his custom to carry crackers and eat them when the gnawing became more pronounced.

It may be said for many years the patient has been spare of build and rather gaunt, although quite strong. The pain became so severe and constant that he decided to come to Philadelphia to secure relief. On the morning of December 18, 1900, he arose early, partook of a light breakfast, and drove to Annapolis, a distance of fifteen miles. He arrived in Philadelphia at the office of Dr. D. Murray Cheston about 4.15 P.M. On examination Dr. Cheston found a tumor about the size of the fist to the right of the median line, just below the margin of the ribs. Further examination was postponed until the evening, when it was arranged the writer should see him in consultation.

At 5 P.M. the patient repaired to a restaurant to take his first food since early morning. At this hour he took a glass of soda-water. He was at once seized with violent pain in the epigastrium and fell on the floor in a faint. He vomited and symptoms of collapse rapidly followed. He was removed to Dr. Cheston's office, where Dr. Morris saw him suffering from severe general pain and collapse. Dr. Cheston saw him at 6.15 P.M.

The previously described tumor had disappeared. The pulse was 120; temperature, 97°. The abdomen was hard; the pain was general. The

writer saw him at 8 P.M., having the good fortune to have the conjoint advice of Drs. Murray and Radcliffe Cheston. The condition was as indicated above. The writer was impressed with the extreme board-like rigidity of the flat abdomen. It was impossible to make any impression. The epigastrium was tympanitic. The pain was extreme and complained of in many situations. The patient complained of intense heartburn, indicating some hyperacidity. There was no vomiting; some retching occurred, when œsophageal and faucial burning was extreme.

The diagnosis of perforation of a gastric ulcer was made because of, first, the history of the case; second, the presence of a painful and tender tumor which disappeared suddenly; third, the onset of acute pain and collapse; fourth, the hyperacidity; fifth, the absence of signs of affection of the gall-bladder or the appendix or of pancreatic disease. Pancreatic hemorrhage and acute pancreatitis were considered possible, though not probable, because of the signs of tumor antecedent to the perforation and because of the absence of the more prominent symptoms of pancreatic hemorrhage—tumor and tympany.

It was our belief that general peritonitis was advancing rapidly, in spite of the subnormal temperature, because of the general pain, the increased pulse-rate, and the rigidity of the muscles.

It remains to explain the presence and disappearance of the tumor. Without doubt perforation had occurred slowly and a localized peritonitis had set in. The sudden pain and shock were due to the giving way of adhesions and the outpouring of the stomach contents into the peritoneal cavity. With this accident the tumor disappeared.

It was fortunate for the good fellow, no doubt, that he had a long fast preceding perforation; that the opportunity for immediate operation could be afforded, and that six and one-half hours after perforation his peritoneal cavity was being cleansed with hot salt solution.

Dr. H. R. Wharton presented the following notes upon the case:

The previous history of this case has been given by Dr. J. H. Musser. I saw the patient on the evening of December 18, 1900, four hours after a sudden attack of pain in the epigastric region, which caused him to faint. When I saw him he was suffering excruciating pain, which he referred to the abdomen. He was slightly nauseated and was making ineffectual attempts to vomit. The temperature was 97°, the pulse 120. The abdomen was not markedly distended, but the abdominal muscles were so rigid that it was impossible to palpate any of the abdominal organs. He could not locate any especial point of tenderness, but complained loudly of severe pain all over the abdomen.

After consultation with Dr. D. M. Cheston, Dr. R. Cheston, and Dr. J. H. Musser we decided that he was probably suffering from a perforated gastric ulcer, and decided that an operation was advisable.

He was removed to the Presbyterian Hospital, and six and one-half hours after his first attack of pain an anæsthetic was administered and it was decided to open the abdomen in the epigastric region, as the symptoms pointed strongly to a perforated gastric ulcer.

When the patient was fully under the influence of the anæsthetic it was noticed that the rigidity of the abdominal muscles was only slightly diminished. An incision three inches in length was made from the tip of the ensiform cartilage toward the umbilicus, and as soon as the peritoneal cavity was opened it was found that a quantity of thin, opaque, purplish fluid escaped. The incision was slightly enlarged and the surface of the stomach was exposed. This organ was grasped and partly removed from the abdomen and carefully examined for the presence of a perforated ulcer. The greater curvature, the lesser curvature, and the anterior and posterior surfaces were carefully examined and no ulcer was discovered. The stomach was replaced and the gall-bladder next examined, thinking that this organ might have been ruptured, as masses of bile-stained mucus were noticed floating in the abdominal effusion. The gall-bladder was found intact. The ascending colon was next sought for and drawn upward, and the appendix inspected and found normal in appearance. The abdominal effusion was next removed by sponging, and it was then noticed that a small amount of fluid still continued to escape from the region of the pyloric end of the stomach. The stomach was again examined by drawing it outward, so that the posterior portion of the pyloric extremity was exposed to view, and there was disclosed a round opening, about one-eighth inch in diameter, from which fluid could be seen to escape. The perforation was situated on the posterior surface of the pyloric end of the stomach, about one-half inch from its junction with the duodenum.

Attempts were made to invert the edges of the opening by introducing silk sutures, but as the edges of the ulcer were undermined and very friable the sutures cut through without producing the desired result. There was also more or less induration of the tissues surrounding the ulcer, which prevented the inversion of the edges of the ulcer. I then decided to cover the ulcer by infolding the walls of the stomach by sutures introduced some distance from the perforation. This was accomplished by introducing six sutures of silk, which effectually closed the opening and prevented leakage, and after they were placed and securely tied a few additional sutures were introduced at the ends of the infolded tissue. The abdominal cavity was next very thoroughly flushed with hot saline solution, about three gallons being employed. Two glass drainage-tubes were next introduced, a long one extending downward toward the pelvis, and a shorter one passed upward in the region of the pylorus. The wound was then closed with silk-worm-gut sutures, gauze drains were introduced to the bottom of the drainage-tubes, and a copious gauze dressing was applied over the wound and held in place by an abdominal bandage.

The patient was much shocked during the operation, but reacted gradually. The morning following the operation he was free from pain, his temperature was normal, and pulse was 80. He was given no nourishment by the mouth for three days, liquid nourishment and water being administered by the rectum. After this time milk in small quantities was given by the mouth. A free discharge of bloody serum occurred from the drainage-tubes, which necessitated frequent changing of the dressings. The drainage-tubes were removed on the fourth day, and small gauze drains were substituted for a few days. The patient suffered no further inconvenience and made an uneventful recovery, the sutures being removed from the abdominal wound on the thirteenth day. Four weeks after the operation the patient was discharged from the hospital and returned to his home.

REMARKS BY DR. WHARTON. Since Mikulicz, in 1880, first performed a formal operation for the exposure and closure of a perforated gastric ulcer the procedure has been employed in many cases with most satisfactory results. A large number of cases in which operative treatment has been employed have been collected and analyzed by Mikulicz, Lindner, Barker, Weir, Lund, Mitchell, Tinker, and Keen, and as the result of their studies much valuable information as to the most frequent site of the perforation, the prognosis, diagnosis, treatment, and the details of the operation have been added to surgical literature.

Perforation is comparatively infrequent in gastric ulcer, occurring according to various observers in from 6.5 per cent. to 18 per cent. of all cases. In Tinker's collection of 232 cases only 22 cases of operation for perforation occurred in the United States. This accident is five times more frequent in women than in men. As regards the results of operations in Tinker's and Finney's combined collection of 268 cases, 139 recovered and 129 died, giving a mortality of 48 per cent. In Tinker's collection of cases operated upon within twelve hours of the perforation, 75 per cent. recovered, and in a late collection of cases 83.78 per cent. recovered. All observers agree that the best result is apt to follow in cases in which a short time only exists between the perforation and the operation.

The ulcer is more commonly situated upon the posterior wall of the stomach than upon the anterior wall, in the proportion, according to Pariser and Lindner, of 190 to 10, and is much more frequent near the pylorus than at the cardiac end of the stomach. Mayo



Robson has observed that chronic ulcers are usually situated near the pyloric extremity of the stomach.

The possibility of more than one perforation should not be lost sight of, for statistics show that in 20 per cent. of the cases this condition was present.

Death from perforated gastric ulcer results from peritonitis, caused by the bacteria which escape from the stomach into the peritoneal cavity at the time of perforation. Richardson considers that the size of the perforation, permitting a rapid escape of the stomach contents, is an important factor in the development of a rapid form of peritonitis, producing, as he describes it, "a sudden overwhelming of the abdominal cavity rather than a spreading invasion."

The ideal method of closing the perforation is to excise the edges of the ulcer and bring them together by sutures. This, however, is only possible in exceptional cases, and in the great majority of cases infolding the walls of the stomach over the ulcer by sutures is the procedure which can be most rapidly and safely practised. Irrigation of the abdominal cavity and careful sponging have both been employed, but, in my opinion, thorough irrigation is the safer procedure: drainage, either by glass tubes or gauze, is usually required, and pelvic drainage should be provided for, either by long tubes or by a counter-opening near the pelvis.

## DEMONSTRATION OF BLOOM'S APPARATUS FOR ARTIFICIAL RESPIRATION.

BY W. W. KEEN, M.D.

[Read February 6, 1901.]

I DESIRE to present to the Fellows an instrument which is a modification of the Fels-O'Dwyer apparatus, and I think a very great improvement over it. At the coming meeting of the American Surgical Association, Dr. Matas will present a modification which he thinks is a still further improvement.

I had occasion recently to use the original Fels apparatus in the removal of a large sarcoma of the ribs which necessitated an extensive opening in the wall of the chest. The work would have been much facilitated could I have had this particular apparatus. It is a very simple one, consisting of a bellows which is worked slowly fifteen or eighteen times a minute to maintain artificial respiration. If it is desired to administer an anæsthetic such as chloroform this can be done by means of a funnel and a little cotton on which the anæsthetic is poured.

The apparatus is connected either with a face-piece, or with a modified O'Dwyer intubation apparatus. The latter is inserted between the two vocal cords so as to close the aperture of the larynx. When the bellows is used the air is forced in; expiration takes place through the tube at the end.

I am quite sure that in two respects the instrument is extremely useful: (1) In surgical operations, as is well shown in Parham's paper on "Tumors of the Chest-wall," in which he used this apparatus. He also has shown the various steps by which the apparatus for artificial respiration has been evolved. (2) Another use

is for medical men. This has even a greater field than the surgical use, because sarcomata and other tumors of the chest wall are rarely seen, but cases of opium poisoning or other conditions in which forced respiration is of the utmost value are very common, and this apparatus will come into use very frequently.

# AN EXPERIMENTAL RESEARCH INTO SURGICAL SHOCK AND COLLAPSE.

By GEORGE W. CRILE, M.D.,  
CLEVELAND, OHIO.

[Read by invitation, March 6, 1901.]

MR. PRESIDENT AND FELLOWS OF THE COLLEGE OF PHYSICIANS: I appreciate more than I can express the honor of addressing this distinguished body. I shall present a part of the summary of an experimental research into surgical shock and collapse. The data has been carefully collected, and by your permission I shall introduce a sufficient number of stereopticon views to illustrate the subject. The experiments were for the most part upon dogs, under surgical anæsthesia. Great care was taken to prevent suffering, and only such number of animals were used as was found necessary to supply the data required. The methods employed were those in vogue in the physiological laboratories.

## SUMMARY OF EXPERIMENTAL EVIDENCE.

### *Tissues.*

SKIN. Cutting and tearing caused in the greater number of instances a rise in the blood-pressure, though sometimes no effect was observed. On blood-pressure, excepting over the testes, and in many cases over the abdomen, there was usually a fall in the pressure; late in the experiment not infrequently there was a fall. The rise in pressure was begun after the lapse of a few heart-beats, and ascended rather abruptly until the highest point was reached, when, after making a rounded crest, it fell again to the level it was before, or below this level; occasionally it remained higher.

On incising the skin over the testes there was frequently a fall in the pressure, in keeping with the phenomena attending injury of this organ. Burning the skin, including that over the scrotum, caused uniformly a marked rise in the pressure. While the peripheral pressure usually paralleled the central, it sometimes exhibited a contradictory movement in point of effect, and not infrequently it differed from the central in point of the time of its movement, though the tendency of the movement may have been in the same direction as the central pressure. This was construed as indicating separate vasomotor effects—*i. e.*, separate from the effect of the heart's action. Respirations were usually slightly accelerated and arrhythmic, though sometimes not appreciably affected. Burning the skin caused increase in respiratory action, sometimes a hyperpnoea. Mechanical or thermal injury of the skin covering the paws caused much greater circulatory and respiratory changes than like injuries in other regions of the skin. All the observations tend to show that the more specialized and abundant the nerve-supply to a part the more will it contribute to the production of shock when subjected to injury. In a series of cases in which preliminary excision of the stellate ganglia was made no alteration in the blood-pressure on repeating the experiments was observed.

**CONNECTIVE TISSUE.** No evidence was found of an appreciable effect from mechanical or thermal injury to connective tissue, fascia, tendons, ligaments, etc.

**MUSCLES.** Cutting or crushing muscles was attended by practically the same phenomena as described under the heading of skin, but to a much less degree. In many instances extensive cutting of muscles caused no appreciable change. As a rule, the simple skin incision in a hip-joint amputation had at least as much effect upon the circulation and respiration as cutting the entire muscular mass of the thigh. No difference could be determined in the various skeletal muscles.

**BONES.** *Periosteum.* In several instances roughly separating the periosteum from the bones caused a small rise in blood-pressure similar to that observed in injury of the skin and muscles; in other instances no effect was noted. Sawing through bone whose periosteum had not been previously removed sometimes was attended by a slight rise in pressure and corresponding respiratory changes; but sawing, cutting, crushing, and breaking bones

whose periosteum had previously been removed was not in any instance attended by any alteration in either the blood-pressure or the respiration. The same may be said of cartilage.

**JOINTS.** On cutting, sawing, curetting, or crushing the joints no appreciable effect was noted. The same may be said of opening the hip-joints and other large joints and doing the various surgical operations thereon.

**NERVE TRUNKS.** *On Circulation.* Crushing, tearing, contusing, or cutting with dull instruments causes usually more or less rise in pressure, followed by a fall occasionally to the former level, but usually lower. Sometimes there was a very great decline below its former level. Vasomotor curves frequently become more prominent just after the curve of stimulation. By repeating the irritation the mean blood-pressure, losing somewhat after each experiment, suffered depression in proportion to the intensity and duration of irritation. In some instances, especially in observations after repeated irritations had been made, there was an immediate decline in pressure; the decline was usually quite gradual, and continued longer than the upward tendency in other instances. Severing the nerves quickly with sharp scissors usually gave comparatively little effect; if a rise, it was but momentary; if a fall, it was immediate, and usually was not recovered from. The total disturbance was decidedly less in quickly severing with sharp instruments than in contusing, tearing, dragging, etc. Electric and thermal irritation both caused curves very similar to though more marked than mechanical irritation.

The peripheral, the arterial, and venous pressures, in the femoral artery, femoral vein, carotid artery, and jugular vein, in the greater number of instances partook of the general movements of the central pressure. In some instances there seemed to be independent action, similar to that described under the heading skin. In cases in which the stellate ganglia had been removed there was usually no change in any of the pressures on the application of the above-mentioned tests, neither was there usually any change in cases in which the cardiac branches had been previously severed. In several instances there was a slight rise, and in a few some fall on the application of the stimuli. However, the contrast, even in the apparent exceptions, was striking—*i. e.*, there was but little alteration in the circulation in the cases sub-

jected to preliminary excision of the stellate ganglia. After the animal had become very weak, or after repeated irritation of the given nerve trunk, there was sometimes a fall without any preliminary rise. In some cases in which cocaine or eucaine had been injected and but little time had elapsed, say only a minute, there was a fall. The nerve trunks referred to are the peripheral only.

*On Respiration.* There was usually an alteration in rhythm; irregular amplitude, short strokes and long strokes followed each other in disorder, as did also overinspiratory and overexpiratory tonus; but, on the whole, the total action is decidedly increased. Normal respiratory rhythm is usually promptly restored on cessation of stimulus. In cases in which there was subsequent effect it was usually manifested by a slow rhythm, with either diminished or increased amplitude. This refers to nerve trunks of extremities only.

In all, forty-three observations were made.

### *Regions.*

**HEAD.** *Nose.* Mechanical injury of the nares, involving contusion, laceration, and dilatation, and in some instances crushing of the turbinated bones, caused a distinct rise in the central blood-pressure, the ascent of the curve being not so sharp as in similar injuries of the extremities. No separate vasomotor effects were observed. Respirations were slowed and the amplitude diminished in most instances. An exception in the way of an increased depth was occasionally noted. Thrusting the finger into the posterior nares and imitating forcible removal of a tumor caused in some instances a partial inhibition of the respiration and of the heart.

*Eyes.* Mechanical injury of the conjunctiva, of the structures of the orbit, of the eyeball, and of the optic nerve occasionally caused a little, though usually no appreciable, change in either the circulation or the respiration.

*Ears.* The external ear, when any effect was noted, produced such alterations as were described under the subject of skin. On contusing, puncturing, and otherwise destroying the structure of the internal ear there was usually a fall in the central, portal, and cephalic pressures, and a rise in the peripheral venous; in one in-

stance there was a fall in the portal only. In the other instances there was a rise in the blood-pressure, and in but one was there any effect on the respiration, a diminished frequency, and depth.

*Mouth.* On crushing, tearing, and puncturing the tongue there was no effect on either the circulation or respiration; on forcibly dragging the tongue out of the mouth there was partial inhibition of the respiration and heart. No effects were observed on operations on the buccal cavity. Crushing the jaws by turning down the screw-clamp of the dog holder produced no appreciable effect. After the jaws had been placed in the position of their maximum normal separation, by applying considerable force in further separating them, respirations were considerably inhibited, and the heart strokes took on a slight "vagal" character—*i. e.*, the frequency was diminished and the length of stroke decreased. On sawing through the median line of the lower jaw, then separating the severed sides laterally from each other, there was a very sharp and considerable rise in the blood-pressure, with decided acceleration of the heart. This was repeated a number of times, sometimes moving them singly, sometimes moving both laterally outward, and it always markedly altered the blood-pressure and partially inhibited the respiration. In one instance, in an extreme outward and upward displacement, there was a decided cardio-inhibitory effect. In no instance was the condyle dislodged from its articulation. These effects were very probably due to stretching or other mechanical injury of the nerves governing the respective functions whose disturbance was observed.

*Pharynx.* Mechanical injury of the vault of the pharynx, the soft palate, the velum, tip and upper surface of the epiglottis and base of the tongue produced varying effects. The under surface near the base of the epiglottis and the superior laryngeal opening caused respiratory arrest on even very slight irritation. On more vigorous digital manipulation there were cardio-inhibitory effects as well. As to the remainder of the pharynx, excitation of swallowing was noted in a comparatively small zone of the lower pharynx, extending just above and below the level of the superior laryngeal opening. Dragging on the soft palate slowed the respiration. In some instances in which very considerable roughness of manipulation was practised on the vault and soft palate there was very marked slowing of respiration and of the heart-beats.



**BRAIN.** *Dura Mater.* Gentle separation of the dura mater from the skull was attended by but little effect. *Hemispheres.* Cutting out the cerebral hemisphere caused a marked fall in the central and a rise in the peripheral arterial blood-pressure.

There was a very striking irregularity in both the blood-pressure and respiration. These experiments were attended by a considerable loss of blood. Respirations failed during the removal of the hemispheres. Gunshot wounds of the hemispheres caused sometimes enormous sweeping "vagal" heart-beats, sometimes an acceleration, usually the former. Respiration in every corresponding case was instantly arrested and rarely resumed. In two instances, after the elapse of some time, very slow and shallow respiratory efforts were noted. Ten observations were made on the effect of rapidly applied pressure within the brain, as might occur in sudden hemorrhage. In each case the heart-strokes took on a "vagal" character, and the respirations failed first. The method employed consisted in making a very small opening into the skull, through which a slender glass canula connected with a pressure bottle of normal saline solution was connected. The canula was passed into the lateral ventricle and the solution allowed to flow. The respiration rapidly failed in each instance, and the heart continued beating, exhibiting very striking "vagal" strokes. The production of depressed fracture by a hammer blow caused instant failure of respiration; the heart beat on strongly for a short time, then failed. Blows not severe enough to cause fracture, but a considerable jarring, caused occasionally a sweeping heart-beat and a temporary arrest of respiration. Pressure upon the surface of the brain produced like results. Mallet blows, if rather severe, produced marked disturbance in respiration and in the cardiac action. Injury of the medulla caused a momentary rise, followed by a staggering fall of the blood-pressure to zero.

**NECK.** *Trachea, Larynx, and Esophagus.* *Larynx.* Contact, even slight, with the mucous membrane of that portion of the outer margins of the superior laryngeal opening, including the under surface of the epiglottis, caused instant respiratory arrest under surgical anesthesia. In cases in which contact was prolonged the respirations gradually resumed their normal rhythm. In cases in which contact was made more firm, as in dilatation of the larynx or compression between extralaryngeal and intra-

laryngeal force, in addition to the respiratory arrest there was partial or complete inhibition of the heart. On continuing intralaryngeal contact tolerance was acquired. Severing the inferior laryngeal nerves did not prevent the appearance of the above phenomena; severing the superior laryngeals abolished them; hypodermic administration of atropine prevented the cardio-inhibitory effect of such manipulation. Cocaine thus administered had a like effect. Neither drug, however, so employed prevented to any appreciable degree the respiratory inhibition. Cocaine locally applied, even in  $\frac{1}{2}$  per cent. solution upon the laryngeal mucosa, within thirty seconds entirely prevented the respiratory and cardiac inhibitions on repeating a like manipulation. The larynx might then be cut, stretched, contused, and otherwise injured without any manifest inhibitory effect on either the respiration or the heart action. In various injuries and operations upon that portion of the larynx inferior to the inhibition area above described, and all the accessible portions of the trachea, no effects were noted. The same may be said of the œsophagus, excepting the dilatation of the latter, which had a variable effect. In one case sharp rise in pressure and irregular, shallow respirations. In five other tests there was observed a temporary fall in blood-pressure, with diminished pulse volume, probably mechanically produced; the respiratory movements were increased in amplitude. Performing operations such as œsophagotomy, and inflicting injuries as stab and gunshot wounds, produced no observable effects on either the circulation or respiration.

*Other Tissues of the Neck.* When proper respect was paid to the vagi and the sympathetic nerves, extensive dissection was made without disturbing either the circulation or the respiration, but mass traction on the wound, or forcible blunt dissection of the deeper tissues, usually caused cardiac or respiratory inhibition, or both. This is especially true of the upper portion of the neck on a level with the larynx and above it, including the region below and behind the angle of the jaw. The so-called "blow upon the jugular," in sporting parlance, owes its effect to the mechanical stimulation of the vagus, thus inhibiting the heart. After preliminary administration of atropine or section of the vagi distal to the point of injury no inhibitory effects were produced. In two instances, however, a rise in blood-pressure with

an acceleration of the beat was observed, in other observations the typical long, sweeping "vagal" beats appeared. The blows in the former instances probably missed the vagus and stimulated the sympathetic. Gunshot wounds of the neck have no effect aside from a momentary one, excepting as they may injure the vagus, the sympathetic, or the "inhibition area" in the larynx. Firing a shot through the thyroid cartilage has but a transitory inhibitory effect. Through the "arrest" area there was temporary inhibition of respiration and "vagal" strokes of the heart. Grasping the neck, as in powerful choking or strangling, caused inhibition, partial or complete, through irritation of the "inhibitory" area of the larynx or traction on the superior laryngeal nerves. It was quite difficult to produce sufficient mechanical injury of the vagi by grasping the intact neck to cause any inhibition.

**THORAX.** In resection of the ribs, fractures, stab wounds, gunshot wounds, etc., in experiments in which the thoracic cavity was not opened, there was merely the effect of such injuries of skin, muscle, and bone. Injury of the skin in this region did not produce so profound changes as in that of the foot and leg. Respiration, however, was considerably affected in rhythm in tearing or cutting the extraordinary muscles of respiration. The tearing and the dragging effects were probably due to a corresponding injury of the supplying nerves. Opening the thorax is attended by the greatest irregularity of breathing—irregular rhythm and excessive action—the blood-pressure undergoes sweeping changes in height, and the heart-strokes usually become short and very irregular. In no other manner were there produced such exceedingly irregular blood-pressure and respiratory tracings as in the intrathoracic procedures. Artificial respirations were, of course, maintained, and naturally interfered with the normal efforts, and, beside, the mechanical factor in operating on the chest wall was considerable. These considerations somewhat lessen the value of the respiratory tracings, but direct observation of the respiratory action made it more probable that the heart action, which was perfectly recorded, was even more disturbed than the respiratory. In resection of the anterior chest wall, by placing a double row of ligatures around the ribs and the sternum, then cutting between the ligatures with bone forceps or saw, and exposing the entire chest cavity by elevating this flap, there was almost immediate normal breathing

and heart action after fastening down the resected wall by tying the corresponding long ends of the ligatures and suturing the skin. Blood-pressure usually suffered a considerable decline during the performance of the manoeuvre. This decline was not due to hemorrhage, as the operation was practically bloodless. This operation was done ten times without death, and, although there was a double pneumothorax, competent normal respiration was in each case restored on closure of the chest. The respiratory action was usually greatly accelerated for a considerable time afterward. However, in experiments in which the chest had been opened there was a tendency to recurring respiratory failure in the subsequent course of the experiment.

**HEART.** The slightest direct contact with the heart caused marked changes in its beat and in the blood-pressure. Touching or gently pressing upon the pericardium over the apex caused a staggering, immediate fall in blood-pressure, with short, irregular strokes. On removal of the contact, blood-pressure immediately mounted again. Likewise, on touching the base and the large bloodvessels near the base, there was a staggering fall in the blood-pressure, with irregular stroke, but a more sweeping stroke than in the apex experiments. Gently displacing the heart laterally caused extreme irregularity, the heart executing a series of most irregular sweeps, with great fall in the blood-pressure. This fall was recovered from upon the release of the pressure. In like manner, pressing up the diaphragm with the hand so as to feel the heart impulse caused phenomena similar to the above, but to a less marked degree. Picking and holding up the pericardium, preparatory to incising it, caused a rise in pressure, followed by a decline: when released there was a very great rise. Incising the pericardium produced but little effect. When the heart had been much weakened, touching or gently moving it caused sometimes complete cessation for a time, then slowly it resumed its beat. Puncturing the heart with a scalpel caused a lapse of one to several beats. A gunshot wound of the heart, not penetrating the chambers, caused but temporary arrhythmia for several beats.

**LUNGS.** Mechanical injury of the lungs in the way of manipulation, contusion, stab wounds, gunshot wounds, etc., on the whole seemed to affect the heart more than the respiration. There was great difficulty in making satisfactory observations on this point.

Some observations showed very marked "vagal" heart-beats on pinching the lungs with the fingers.

**LARGER VESSELS.** The venous trunks especially cause sweeping changes in the blood-pressure by mechanically interfering with the flow of blood into the chambers of the heart, and also in manipulation near the base of the heart the latter's rhythmic contraction is interfered with; probably because the contraction wave at the commencement of each cardiac cycle begins in the venous trunks near the base. In fresh animals there was a prompt recovery of a lost cardiac equilibrium, but not so if the animal had been well exhausted when the equilibrium was disturbed.

**DIAPHRAGM.** Contact, however slight, with the abdominal side of the diaphragm caused in every instance markedly arrhythmic respiration. If contact were extensive every part of the respiratory curve became irregular and fragmentary. Puncture of the diaphragm and gunshot wounds usually caused immediate arrest of respiration, and if the arrest proved to be temporary there was a tendency to respiratory failure later in the experiment. Hot water applied to the abdominal side of the diaphragm very greatly augmented the amplitude of the respiratory movements and increased its frequency.

**LIVER.** Aside from the mechanical effects from forcing blood from this vascular organ by pressure, and the effects of contact with its peritoneal covering, as above indicated, no special effects were observed. Dilatation of the cystic ducts caused no appreciable effect. Manipulation of the gall-bladder caused a marked temporary fall; but it is extremely probable that this was due to mechanical interference with the blood-current in the larger venous trunks lying in such close anatomical relation.

**KIDNEYS.** Cutting, contusing, crushing, or any other mechanical injury of the kidney caused no notable effect in a single instance except when there chanced to be peritoneal contact. The same may be said of nephrectomy performed a number of times.

**SUPRARENAL BODIES.** On similar treatment a rise in the blood-pressure was noted in a number of instances. No separate vasomotor effects were noted.

**SPLEEN.** No special results were noted other than when that organ was compressed. There was an immediate small rise, probably due to forcing out blood from its vascular meshes. Splenec-

tomy was performed a number of times and with practically no effect.

**BLADDER.** Cutting, compressing, overdistending, or otherwise injuring the bladder caused a rise in the blood-pressure, if any effect at all was produced. In many of the observations no effect was noted. Pressure upon the full bladder produced the most marked results.

**UTERUS.** Incision, contusion, manipulation, or any other mechanical injury of the uterus caused uniformly a rise in the blood-pressure. The rise appeared rather tardy, but was in many instances very marked. Sometimes the pressure gradually declined to its former level, but tended to remain for some time at least at the level to which it rose. Repeating the injury at intervals before compensation occurred raised the mean pressure very considerably comparable to the rise caused by clamping the abdominal aorta. Cutting the cardiac branches of the stellate does not prevent the rise. While conclusive proofs were not at hand, there is considerable evidence that the rise is due to vasomotor action. What has been said of the uterus may be said of the ovaries and oviducts, and in importance in the order given. Ten bitches each furnished repeated observations on these points. Cæsarean section was twice made, and noted for the absence of any changes in the pressure during the operation.

**MALE GENITAL ORGANS.** Cutting the testicle, spermatic cord, tunica vaginalis, and frequently even the skin of the scrotum, caused in most instances a fall in the blood-pressure, appearing after a considerable interval. Manipulation, though gentle, of the testicle always caused a marked fall in the central pressure; the same observations were made with regard to the spermatic cord. In fact, any manipulation of any part of the testicle—its coverings or the spermatic cord—was attended by a marked, sometimes an exceedingly great fall, in blood-pressure. While the central pressure was falling the portal was usually as markedly rising as evidence of splanchnic dilatation as the cause of the fall. The blood-pressure usually recovered completely or nearly its former level. These observations were made fifty-three times, and occasionally, though rarely, no fall was marked. Respirations were slowed and shortened and in some instances irregular. Injecting cocaine into the organ, into the tunica vaginalis, or into the sper-



matic cord after a control had been obtained, then repeating like operative procedures, no fall occurred in central and no rise in portal; neither were the respirations altered. Following an injection of sufficient amount of atropia into the jugular vein after severing an inhibitory laryngeal control, thus proving the atropia competent to abolish cardio-inhibitory impulses, the testicle was subjected to experiments similar to the above, and the usual fall in pressure followed. The fall was not prevented by preliminary section of the vagi. This is taken as evidence that the fall is probably not due to a cardio-inhibitory effect. Jugular injections of cocaine did not prevent the fall in the pressure, though as nearly as could be judged the fall was considerably less than in the controls.

**PENIS.** The same may be said of the penis, though the alterations were not observed to be produced in nearly so marked degree.

**VAGINA.** Forceibly dilating or otherwise injuring the vagina caused an increase in depth and frequency of the respirations and usually a rise, though occasionally a decline in blood-pressure. In several instances there was no effect on blood-pressure, but **respiratory action was increased.**

**ANUS.** Forceibly stretching the rectum and anus caused sometimes a rise, sometimes a fall, in blood-pressure, and an increase in the frequency and depth of respiration. There is considerable evidence that the fall in pressure was due to mechanical interference with the flow of blood in the venous trunks, viz., the fall appeared almost instantly, and the manometer in the femoral vein showed a rise at the same time that the central was falling.

**EXTREMITIES.** Cutting, crushing, fracturing, amputating, and burning the extremities were usually attended by a preliminary rise in blood-pressure, followed by a fall usually lower than before the operation. Respirations were much altered in rhythm and temporarily increased in frequency. There is no evidence of the correctness of the opinion expressed by many clinicians that there is considerable shock produced in sawing through the bone in amputations, nor of similar opinions as to opening large joints. The error probably arises in confusing the effects of cutting, traction, or other injury of the nerve trunks, which would be clinically manifested about the time a rapid operator would have proceeded to sawing the bone or opening the joint in a hip-joint amputation. Traction on the nerve trunks especially caused

marked effects upon both respiration and circulation. The shock is in direct proportion to the amount of excitable tissue injured and the time occupied in the operation. The experiments on which these observations are based were made without loss of blood. Injury of the paws is more productive of shock than that of any other superficial part of the extremities. There is sufficient evidence to show that the shock produced is in direct proportion to the nerve-supply and to the functional importance of the part injured. In operations involving the brachial plexus the respiratory changes were very striking, the frequency of respiration was much increased, and overanæsthesia was accordingly produced unless the anæsthetic was removed. Operations involving the brachial plexus produced also very marked vasomotor disturbance, as shown by the peripheral manometer and by the Traube curves in the central blood-pressure tracing.

Collapse or death produced by blows upon the lower chest and epigastrium were found to be due to the effect upon the heart and not the solar plexus. No amount of injury inflicted upon the solar plexus did in any instance produce collapse. The immediate effect of a blow upon the lower chest or upper abdomen is an injured heart action and lower blood-pressure, after which, if the blow is not too severe, recovery takes place.

A research into the mechanism of sudden drowning showed that if the circulation in the lungs were subject to pressure of a column of water equal to or greater than the pressure in the capillaries the entire circulation was immediately blocked. The animals were killed in about fifteen seconds in these experiments. This is the most probable explanation of certain sudden deaths by drowning.

A research into the phenomena produced by the presence of foreign bodies in the pharynx and œsophagus showed that the symptoms were strikingly different in every portion of the œsophagus below the level of the larynx, but that the upper œsophagus and pharynx resemble very closely the symptoms of foreign bodies in the larynx, the reason being that under either case the superior laryngeal nerve or its terminal was subjected to a mechanical stimulation, thereby producing reflex inhibition of the respiration and the heart. Injecting atropine prevented the reflex inhibition upon the heart. In laryngotomy it was found that opening the larynx produced reflex inhibition; in tracheotomy no such



phenomena appeared. This is the explanation of the clinical observation that at the moment entrance is obtained in a laryngotomy the patient frequently died, death being due to reflex inhibition of the heart. The use of cocaine injected by means of a hypodermic needle into the walls of the larynx in laryngotomy and the use of cocaine applied locally upon the laryngeal mucosa prevented inhibitory phenomena. Collapse and death may follow the mechanical irritation of the laryngeal mucosa. This may be prevented by the use of atropine.

Traction on the tongue, if slight, produces little change in the blood-pressure or respiration, but if great traction is produced a reflex inhibition of respiration and sometimes of the heart is produced. This has an important clinical bearing on the dragging out of the tongue in giving anesthesia and in resuscitation.

CONCLUSIONS. As a result of injury or operation there may be immediate or later depression or death. *Immediate depression or death* from injuries or operations was due to one or more of the following factors:

1. Cardiac.
2. Respiratory.
3. Hemorrhagic.
4. Vasomotor.

The phenomena produced by these factors have so many points in common that they naturally fall into a group, and would seem to be appropriately designated as collapse.

Later depressions or death from injuries or operations, and due to a vasomotor impairment or break-down as the essential factor, may be appropriately designated *shock*.

FACTORS PRODUCING COLLAPSE. *Cardiac*. The cardiac factor may be due to:

(a) Injury of the heart muscle, as in gunshot and stab wounds, etc.

(b) Injury or operation involving the vagi or certain of their branches—*i. g.*, a direct blow upon the vagus, intralaryngeal manipulation, etc.

(c) Injuries of the cardiac centres in the medulla, crushing of the skull, etc.

(d) Paralysis of the heart muscle by excessive anesthesia, notably by pushing chloroform or by administering an injection

of the same into the vein; the heart muscle fibre is thus readily paralyzed.

*Respiratory.* This factor may be introduced by:

(a) Injuries or operations upon the thorax, destroying its integrity, thereby producing collapse of the lungs.

(b) Injuries or operations involving the respiratory nerve mechanism—*e. g.*, destruction of phrenic nerves in continuity, cross lesion of the spinal cord above the fourth cervical vertebra, mechanical stimulation of the superior laryngeal.

(c) Injuries or operations affecting the respiratory centres in the medulla as well as the higher respiratory centres at the base of the cerebrum—*e. g.*, excessive intracranial pressure, gunshot wounds, compound fractures, etc.

(d) Mechanical interference with the exchange of gases.

(e) Excessive anaesthesia, whereby respiratory action is arrested.

*Hemorrhagic.* Excessive hemorrhage, especially from the large venous trunks, may cause collapse.

*Vasomotor.* The vasomotor centres are continually in action, and exercise thereby a continuous pressure upon the contents of the bloodvessels. This continuous pressure is known as vascular tone. A cross-section of the spinal cord at any given point produces loss of this vascular tone, thereby permitting the vessels to passively dilate to their utmost, and, if the lesion involves a sufficiently large area of vessels, collapse may be produced, the accumulation of blood within this area of vascular dilatation being practically equivalent to a hemorrhage. The same may be said of sections of such nerves as the splanchnics—nerves that control a capacious vascular area.

It is only this phase of vasomotor influence that may be particularly operative in producing collapse. The vasomotor nerve mechanism may also be paralyzed by an excess of anaesthesia, especially by chloroform.

**SURGICAL SHOCK.** Surgical shock is mainly due to impairment or breakdown of the vasomotor mechanism. All the factors referred to as causing collapse may add to shock. The evidence from which this conclusion has been reached is the following:

Nerve fibres when subjected to stimulation, mechanical or otherwise, may cause either an increase or a decrease in the blood-pressure. The presence of the so-called "pressor" nerve mech-

anism is well established, as is also the presence of the so-called "depressor," and these "pressor" and "depressor" nerve mechanisms have a representation in the nerve trunks. Now, mechanical stimulation of sensory nerves when both the animal and the nerve are fresh produces a rise in the blood-pressure, due largely to a stimulation of the pressor mechanism. On repeating the stimulation of the same nerve each subsequent repetition is attended by a diminished pressor action, and, finally, no effect is produced upon the blood-pressure. On the contrary, there may be a fall in blood pressure after still further stimulation—that is to say, the depressor action alone may appear. Not only is this true with reference to repeated stimulation of the same nerve, but after repeated stimulation of other nerves there will be finally a condition produced in which no stimulation even of a fresh nerve trunk will produce a rise in the blood-pressure; in other words, it would seem that the pressor action may be exhausted in a given nerve trunk by repeated stimulation of different nerve trunks, the latter being general, the former local, in the sphere of its influence. It has been almost universally noted that the development of shock increases *pari passu* with the failure of the pressor action—that is to say, so long as the blood-pressure remained high or fairly high it would be found that the pressure action could be brought out on stimulation of a fresh nerve trunk. On the contrary, after a sufficient number of stimulations there could be a marked lowering of the blood-pressure, and at the same time the pressor action became greatly impaired or entirely abolished. As nearly as could be estimated, the depth of the shock was in proportion to the failure of the pressor action; and when a given nerve or when the entire animal had been reduced to such a condition, further stimulation in many cases produced a primary fall in blood-pressure, and generally without a later compensatory rise. It has been pointed out by others that when a nerve trunk is severed and repair has taken place, a stimulation applied early to the repaired nerve trunk will produce a primary fall in blood-pressure, but such stimulation applied later will produce a rise in the blood-pressure—that is to say, the depressors repair earlier than do the pressors. If a nerve trunk be reduced in temperature to a point at or below zero, then the distal end stimulated, there will be a lowering of the blood-pressure—a depressor action. In this way

the two actions—the pressor and the depressor—are separated. It would appear, then, that the pressor action is brought out on first stimulation or early stimulation, and that the pressor action is more readily exhausted than in the depressor action. The physiological importance of the pressor action is too apparent to be necessary to be entered into here, and the helplessness of the circulatory apparatus when its pressor action has been lost must be complete. In this condition of lost or impaired pressor action the blood is transferred to the venous side, notably to the large venous trunks, all of which are dilated. In a given tracing the volume of blood put out of the heart with each beat is indicated by the stroke of the writing style of the manometer. This stroke in every case was lessened as shock was developed. When the dog board was inclined with the head of the animal downward the blood-pressure underwent a relatively great rise, suggesting the emptying of the blood from the engorged toneless vessels in which it had accumulated. The usual physiological compensation in changing of posture was not manifested in profound shock. In a fresh animal, and when the circulatory apparatus is normal, if an animal be suspended feet downward, there will be an immediate fall in blood-pressure, but directly after there will follow a compensatory rise, so that in a short time the blood-pressure will have wholly regained its normal level and sometimes temporarily rise even above the normal. This has been demonstrated to be due largely to the vasomotor mechanism regulating the calibre of the vessels. In the state of shock (and the phenomena are almost in direct ratio to the depth of the shock), when an animal is inclined feet downward, thereby causing a fall in the blood-pressure, there is but little if any compensatory rise, and in some cases of extreme shock there was no compensatory rise at all. The amount of compensation was believed to be in proportion to the depth of the shock—that is to say, the bloodvessels were so nearly toneless and were so far out of the control of the vasomotor mechanism that their calibre was not altered in the normal process of the compensation, supporting the observations just made that in profound shock there is a loss, partial or complete, of pressor action. It was further observed that if an animal was allowed to partially recover from its condition of profound shock and then inverted there was an inauguration of a compensation

seemingly in proportion to the extent of the recovery from shock. It would then seem that in the fatal cases of shock and in the conditions of most profound shock there is a condition of either total paralysis of the vessel walls or its equivalent.

Negatively, that the heart is not exhausted, and that it is not the principal factor in the production of shock, rest on the following evidence:

The heart muscle itself is functionally characterized by its capacity for work, as athletic exercises, physical endurance tests, etc., prove. An experimental mammalian heart has been made to beat as long as five hours after its removal from the body, having as its circulating medium defibrinated blood. Now, in the condition of shock there is distinctly less work for the heart to do, and the more profound the shock the less the work, estimated by the amount of blood the heart puts out. But it may be asserted that the heart-beats with increased frequency *pari passu* with the development of shock, and its "machinery running empty" runs away with itself, and so becomes exhausted; but in the experiments in which the cardio-accelerator fibres had been previously severed, and the heart in consequence beat slowly until death, a descending curve in the blood-pressure showing the final vasomotor breakdown was practically the same as in the experiments in which the heart ran rapidly until the end. Finally, when the heart had been allowed to so "run down" almost to the point of ceasing, and normal salt solution was allowed to flow into a vein, causing thereby increased venous pressure, hence supplying the heart with more fluid, the heart was at once reduced to slow and full beats, showing that it was not exhausted, and that it beat rapidly because it did not have enough to do rather than that it was overworked. In this condition each heart-beat produced a long stroke of the manometer, the extreme length of the stroke being caused by the combined effect of throwing maximum quantities of blood into the aorta with each beat and the toneless condition of the vessels, so that on account of this toneless condition the increased pressure produced by each individual beat was not sustained, and, therefore, the excursions were extremely long. After a number of these sweeping strokes had been executed and the vasomotor tone was again regained, the general blood-pressure rose, the strokes became more rapid and shorter, approaching

the normal, and at this time vasomotor curves again reappeared. Before this, while by the extraordinary length of the strokes the toneless condition of the vessels was announced, no vasomotor curves appeared. In cases in which the vasomotor tone was not regained the long, sweeping strokes went stalking along until the heart failed to contract, and death occurred in diastole.

The cardiac factor no doubt plays a part in the production of shocks, because a normal cardiac action is essential to the maintenance of the normal blood-pressure, and it is highly probable that the causes producing the depression or breakdown in the vasomotor system also cause an impairment of cardiac action, as has been pointed out in referring to the cardiac factor in shock under that head in the summary. The respiratory factor is also an important one, inasmuch as the respiratory action was noted to have been altered in almost every injury or operation that may produce shock, and the respiratory action is of great importance, equal to or greater than that of the cardiac. Impaired respiratory action would lead to impaired gaseous exchange in the lungs, thereby the vasomotor as well as all other functions would be impaired. But shock was produced in all the experiments in which a sufficient exchange of gases was provided by means of artificial respiration.

The influence of hemorrhage on the production of shock was very marked. It need only be stated to be accepted that the vasomotor system, in adapting the calibre of the vascular system to the needs of the circulatory apparatus so as to maintain a mean blood-pressure, has adjusted itself to a normal quantity of blood. If, then, there is a hemorrhage there will be an additional stress laid upon the vasomotor mechanism to sustain a mean blood-pressure with a diminished volume of blood upon which to act. The mechanism, then, is at the disadvantage of having called out a part of its potential energy, leaving less with which to meet emergencies. This would be true of capillary hemorrhage as well as arterial or venous hemorrhage. In the latter, however, the effect is more sudden; and it was noted in cases in which there was considerable loss of blood, even though the general blood-pressure had suffered but slightly and only temporarily, that such animals, so far as comparative observations permitted a deduction, did not sustain operative procedures calculated to produce

shock so well as animals in which such loss of blood had not occurred.

Then, again, the anæsthetic factor is of very great importance, inasmuch as while the vasomotor mechanism is contending against the causes which tend to impair or destroy its action, if a part of the possible energy of the vasomotor system is lost by the effect of anæsthesia, it will be readily seen that to this extent the vasomotor centre is impaired, and in the cases in which the anæsthetic was too rapidly administered there was in direct proportion a rapid development of shock.

Surgical shock, then, is due mainly to a vasomotor impairment or breakdown. The cardiac and the respiratory factors may be of considerable importance. However, the main effect is on the vasomotor mechanism.

If the foregoing be true, it will be seen how much more important is prevention than treatment. Prevention of shock may best be accomplished by taking into account all the known physiological functions of every tissue and organ of the body in a way that would suggest itself to any practical surgeon. While the cause may be local, the treatment must be general. It would seem to be desirable to direct special attention to the distinction made between collapse and shock.

The result of action is reaction; of rest, is restoration.

## DISCUSSION.

DR. BRINTON: I would like to ask Dr. Crile if in his investigations he has ever found any great degree of shock to follow manipulation of the thyroid gland, and especially of its isthmus, whether by ligation or division of the latter, or both?

A great many years ago, in a case of laryngo-tracheotomy for a foreign body impacted in the larynx of a boy, about ten years of age, I ligated and divided the isthmus. This was instantly followed by cessation of respiration, disturbed action of the heart, and a state of intense shock, from which the patient was with difficulty extricated only after artificial respiration and the free use of diffusible stimulants. This case made a deep impression on my mind, and I was entirely satisfied that the trouble was due to the division of the isthmus structures. Following this experience, I made frequent dissections of the human thyroid isthmus—several on the bodies of



children. All that I could find was the distribution in, and over the isthmus of fibres of the sympathetic nerve in greater or less abundance. In later years I have carefully watched, as opportunity offered, the effect of surgical interference with the thyroid isthmus, and I have repeatedly, though not always, seen this to be followed by sudden shock, more or less intense. In one or two cases a disastrous result was undoubtedly referable to the division of the isthmus.

DR. CHARLES H. FRAZIER: While listening to Dr. Crile's remarks concerning his investigations and observations upon shock, which were all made upon dogs under chloroform narcosis, I have been wondering whether he has carried on any experiments under spinal anæsthesia. Ever since the introduction of this form of anæsthesia, which seemed to me to open up an enormous field for research work, I have had it in mind to direct a series of experiments bearing more or less directly upon the subject of shock. It had seemed to me that could we eliminate the effects of ether or chloroform narcosis by substituting therefor spinal anæsthesia, the results obtained in our investigations would be much more positive and reliable. Before, however, any conclusions can be drawn we must have some knowledge as to its effect upon the blood-pressure, the body-heat, the circulatory and respiratory apparatus, etc. As far as I know but little work has as yet been done along this line. Hallion and Tuffier have studied by suitable technique the effect produced upon the circulation of a dog by the intraspinal injection of cocaine. While this alkaloid introduced into the bloodvessels or into the cellular tissue *raises* the pressure and produces a general vasoconstriction, these observers report that the subarachnoid injection of cocaine in the lumbar region always caused a *lowering of* arterial tension, which followed a vasomotor paralysis of the whole subdiaphragmatic tract. They found that the arterial tension could always be brought to its original pressure, either by exciting the splanchnic nerves or by compressing the abdomen. I should like very much to know if Dr. Crile employed spinal anæsthesia in any of his experiments, and what results he obtained.

DR. WILLIAM J. TAYLOR: Dr. Crile has said that after the vasomotor disturbance has reached a certain point there is nothing in the way of treatment which will be of any advantage. I would like to ask whether, from his experience, he can give us any method of treating shock after this great vasomotor disturbance has occurred.

DR. GEORGE ERETY SHOEMAKER: I should like to ask Dr. Crile whether his experiments in the manipulation of the testicle and ovaries have been carried to the extent of crushing in both instances. I am interested in the question of the rise of blood-pressure obtained in the doctor's experiments, because during operations I have been carefully avoiding clamping or crushing the ovary in order to avoid shock. Direct pressure with the finger on a prolapsed ovary may produce nausea, as will similar



pressure on the testicle. Physiologically the ovary is in a position to receive a certain amount of pressure during parturition or from fecal masses, and it is interesting to learn that such pressure does not lower the vital forces.

DR. JOHN G. CLARK: There are two lines of research, one of which has a purely scientific value and the other a practical bearing. The latter is always of greater interest to me, for I prefer scientific work which assists us in the treatment of our patients. Dr. Crile's experimental work is of this character, and is, therefore, of the greatest interest to every surgeon. He has apparently covered the ground in a very thorough way, and, therefore, in discussing his paper one can only pick out here and there points for inquiry.

I have of recent years been convinced more and more that the shock following surgical operations is in the large majority of cases due to profuse hemorrhage during the operation or to a slow oozing or bleeding after the operation. This would, of course, be in line with Dr. Crile's explanation, for it would be simply lack of vasomotor resistance incident to the decreasing volume of the blood due to the hemorrhage. The results of his experiments in the manipulation of the peritoneum are interesting. Whether the depression incident to the manipulation of the peritoneum noted in his experiments is likewise observable in the human individual is a question, for we know that operations may sometimes be prolonged for a considerable time, even when there is rather extensive traumatism to the peritoneum, without any marked depression to the patient. Thus, for instance, in radical operations for cancer of the uterus, in which the patient is on the table for two hours or longer, there may be no serious depression noted until almost the completion of the operation. At this time, however, it may be comparatively rapid in its onset. The pulse, which may have been running at 100 or a little higher, may become more and more accelerated until it reaches 160 or higher. I have noted, however, that even in these cases, with the use of saline infusions, or of large quantities of salt solution, left in the peritoneal cavity, a rather rapid fall in the pulse. Thus, time after time, I have seen patients leave the operating-table after these operations with a pulse barely perceptible, and with the use of the saline infusion the pulse would quickly become perceptible and drop to perhaps 100 within two or three hours.

Under these circumstances the question naturally arises whether this depression at the completion of the operation is incident to the manipulation and the exposure of the peritoneum, or whether it is simply due to excessive radiation of heat during the prolonged operation. If there is this depression which Dr. Crile notes in incising the peritoneum, the question arises in my mind as to whether the patient, as it were, becomes immune to the traumatism and gradually reacts until the normal point is again reached before the completion of the operation.

What the speaker has said concerning the shock incident to the manipulation of the pharynx and larynx is again, I think, of particular interest. There are numerous methods of resuscitation employed in cases of ether asphyxiation. A frequent complication of etherization is the accumulation of mucus in the tracheal and bronchial tubes, causing more or less cyanosis and filling up of the pharynx with thick tenacious mucus.

As a resuscitation measure, or perhaps as a means of clearing the pharynx of this mucus, I have frequently seen the tongue dragged forward with forceps, or even a barbarous-looking skewer or needle thrust through the tip of the tongue, upon which traction is made, while the assistants vainly endeavored to clear the blood and mucus with a sponge pushed down into the throat. Personally I have never seen any good come from this, and I feel that in some instances serious harm may arise by causing even a greater depression of the patient.

In view of the general character of Dr. Crile's investigation, I feel that to discuss it intelligently one must study it more carefully, and, therefore, the remarks which I have made are merely incidental, and, as I have stated in the opening of the discussion, are rather in the form of inquiries than in any sense a criticism.

DR. COOPER, of Edinburgh, begged to be allowed to express his indebtedness to Dr. Crile for his interesting and instructive paper, and drew attention to the many difficulties to be encountered in connection with such work in England.

DR. G. G. DAVIS: The experiments of Dr. Crile in relation to the effect upon the blood-pressure by traction upon the tongue in regard to methods of resuscitation are very interesting. If I understood him rightly, sudden death by drowning is not due to suffocation, but to stoppage of the circulation; also, that the traction of the tongue caused a very marked fall of blood-pressure. It did not cause any rise in blood-pressure. A few years ago it will be remembered that Dr. Laborde, of Paris, in an article on methods of resuscitation, strongly advocated his method of rhythmical traction of the tongue as a means of restoring people who have been drowned. If Dr. Crile's view is correct, that death is due to a lowering of blood-pressure, I can hardly see how it is possible for a measure which tends to lower blood-pressure, as Dr. Crile has shown traction on the tongue to do, will likewise restore a person who has been nearly killed by this very lowering.

DR. CRILE (in closing): In reply to Dr. Brinton's inquiry, I would say that I did experiment on the thyroid gland, but did not obtain any notable results.

In reply to Dr. Frazier, I have done a number of experiments upon the spinal cord, but in spinal anaesthesia operative procedures do not modify the blood-pressure.

To Dr. Taylor's inquiry, I have no theoretical treatment for a patient

whose vasomotor system has gone to dissolution. I have found nothing new in the treatment of shock.

Replying to Dr. Shoemaker, there is nothing more striking to me than the contrast between the effect of crushing the ovary and crushing the testicle. If any effect upon the ovary is produced, it is a rise in blood-pressure; if upon the testicle, there is a fall in blood-pressure, and the character of the rise and the character of the fall are very much the same. It has occurred to me that this whole question of the antithesis between the sexual organs of the two sexes has a number of interesting bearings.

As to cold and heat there is nothing new to say, except a very extraordinary effect which I noticed once or twice when the superficial veins of the skin were much distended. By passing ice over the surface of the body, followed by heat, the two produced a very marked change and brought back the pulse.

In the question of shock and hemorrhage, referred to by Dr. Clark, the most important thing to my mind is that which the circulatory apparatus is able to do. In another series of experiments I have not touched upon this evening I have grouped what has been done in showing how far the circulation is able to compensate for blood loss. A dog may be bled extensively (one-thirteenth of the body-weight) without lowering the blood-pressure. Compensation is obtained by increased action of the heart and increased vasomotor action. There is but a limited amount of potential energy in the vasomotor system. In the course of operation the greater part of the compensatory power may be lost. After any loss of blood shock comes on more rapidly, largely because the compensatory power of the circulatory apparatus has been so much drawn upon to maintain normal blood-pressure. The longer any part is exposed the greater the shock. The tendency of shock is to pass off. It would seem that much depends upon the way the stitches are placed—whether too tight, or whether blood-clot has been left as a foreign body; also whether there are raw surfaces. I have seen nothing like immunity. Some dogs endure a great amount of traumas, while others but little.

Referring to Dr. Davis' remarks upon traction upon the tongue, the theories do seem contradictory. It required considerable traction to produce the inhibitory phenomena. I think it dangerous to produce much traction upon the tongue of an infant. I think the habit of blowing into a child's mouth might be dangerous in the way of blocking the pulmonary circulation. I would not say that the average drowning is due to blocking of the pulmonary circulation, but this may be true of the cases of quick drowning.

I appreciate very greatly indeed the discussion which the Fellows of the College have given.

# NITROUS OXIDE AND OXYGEN AS A SURGICAL ANÆSTHETIC.

DESCRIPTION OF A NEW APPARATUS FOR ADMINISTERING THESE GASES, AND REPORT OF 100 OPERATIONS, THE NARCOSIS LASTING HALF AN HOUR AND UPWARD.

By S. ORMOND GOLDAN, M.D.,  
NEW YORK.

[Read by invitation April 3, 1901.]

IN the use of nitrous oxide in combination with pure oxygen we possess an anæsthetic which must have for every operator a double interest. First, its universal safety ; second, the fact that there is absolutely no physical condition of the patient which contraindicates its use. All will admit that in the interest of the patient the safest anæsthetic should always be selected. This is rarely done at the present time, for the reason that ether and chloroform are in the vast majority of instances considered the only anæsthetics adapted for surgical purposes. In the rare cases where nitrous oxide and oxygen is selected as the anæsthetic, it is a matter of necessity, not choice—that is, because other anæsthetics for various reasons are contraindicated. It might be as well to state right here that where profound and long narcoses are necessary another anæsthetic should be selected, yet as our knowledge increases in the use of this anæsthetic its field for usefulness will greatly extend.

The use of a new anæsthetic or method is usually decried by those who have rarely or never used either. Nitrous oxide is so universally associated with dental work that the surgeon is prone

to imagine it is not applicable to operations of longer duration. Even if he thinks otherwise the old cry of complicated apparatus and great skill, both necessary and hardly obtainable in most hospitals, preclude its use. It is well known that in ordinary gas administration the production of anaesthesia is accompanied with intense cyanosis bordering on asphyxia. Efforts have been made to eliminate these asphyxial symptoms by admitting air in various quantities, but in so doing anaesthesia also passed off, the patient becoming conscious.

The inhalation of nitrous oxide alone has very frequently been said to produce its effects simply by asphyxiation, but while true to a certain extent there is no doubt it has pure anaesthetic properties, and nothing demonstrates this more perfectly than its use in combination with pure oxygen gas. Here asphyxial phenomena are entirely avoided, yet if the gases are actually proportioned perfect surgical anaesthesia can be obtained in most cases.

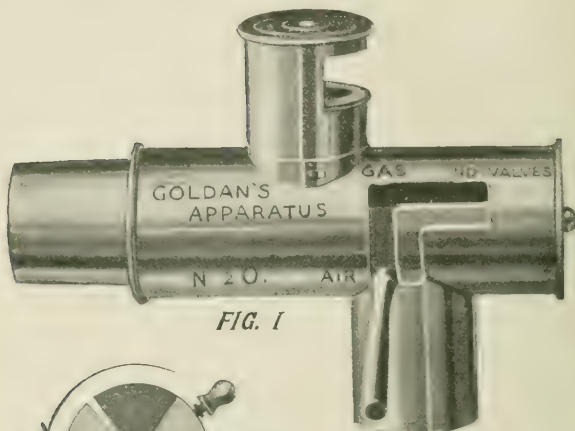
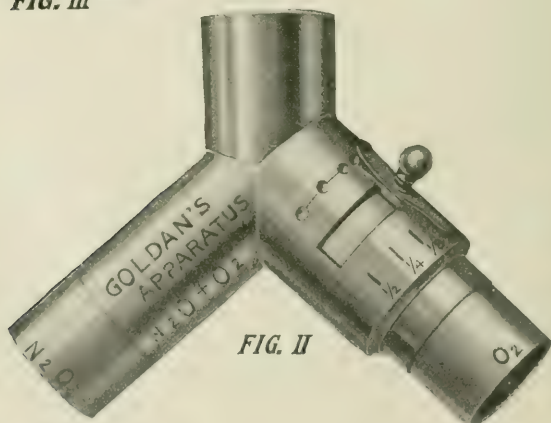
It is perfectly possible to administer gas alone for long operations. I have so used it, but a little thought will convince anyone that this is not an advisable thing to do, especially when we have gas and oxygen. For to anaesthetize a patient more or less cyanosis is necessary, then a breath or two of fresh air is given and the mask reapplied—that is, before consciousness is regained. This continual deprivation of oxygen, it is well known, abolishes metabolism. It may be questioned whether to keep this up for a long time would not be a more serious method than the use of ether or chloroform. Now, the oxygen in the air exists to about only 20 per cent.; 80 per cent. is practically an inert gas (nitrogen); to use this combined with nitrous oxide means, in the first place, we can never increase the gas sufficiently to obtain anaesthesia and at the same time utilize the oxygen to prevent cyanosis. The oxygen can never be regulated; this method must of necessity be one of deep anaesthesia by gas bordering on asphyxiation. In the administration of an inert gas and a small percentage of oxygen—that is, with the patient alternately anaesthetized and conscious, or nearly so—unless the administrator is particularly skilful it cannot be conducted without great discomfort to the surgeon. In short cases the method has no disadvan-

tages ; the surprise is that the dentist alone, and not the surgeon, makes use of it.

It must occur to everyone who administers gas that if a method could be devised by which the oxygen percentage could be regulated by using it pure in combination with nitrous oxide we might have an ideal anæsthetic. Without going into the history of the subject, it is simply necessary to remember that if the inert oxygen can be eliminated the nitrous oxide percentage can be increased just that much ; then by using pure oxygen to the amount of 10 per cent. we can obtain perfect anæsthesia with no asphyxia. Does anything prove more conclusively that nitrous oxide has pure anæsthetic properties ? Practically, it is found that non-cyanotic anæsthesia is obtained by this combination when the oxygen varies between 8 and 15 per cent.

The late Dr. W. W. Van Arsdale, of New York, to whom I am indebted for many practical hints regarding this anæsthetic, used volumetric quantities of these gases in a large number of cases ; this was about ten years ago, when this method of anæsthesia was first attracting considerable attention abroad and here. He said these gases could not be used except in minor cases, the reason being he could not vary his percentages of oxygen ; but he lost sight of two very important practical points—that the same percentage will not answer in all cases, and, furthermore, it must be varied from time to time in the same case. To administer nitrous oxide and oxygen requires a more complicated apparatus than for ether and chloroform. An absolute essential is the undivided attention of the administrator.

While it is possible to accurately determine the exact proportion of oxygen used in this method of anæsthesia, it is not practicable, as several cylinders would be necessary, each having a different proportion of the gases ; then the cylinders would have to be freshly filled, as decomposition is said to take place (Hillischer) when these gases are kept together any length of time, rendering the mixture irrespirable, due to the higher oxides of nitrogen. This method, it can readily be seen, is impracticable. To obviate these difficulties several apparatuses have been devised to administer the gases from separate cylinders, the mixture in varying

*FIG. I**FIG. III**FIG. II*



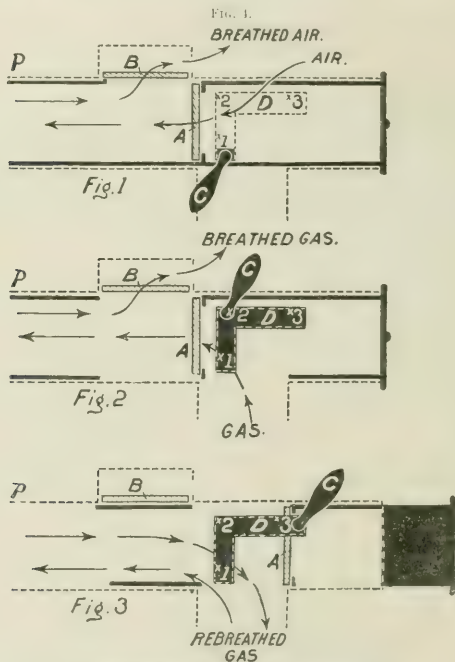
proportions taking place at the time of inhalation. All these instruments give the percentage of oxygen only approximately. We determine the percentage by the condition of the patient, varying, as said before, in ideal narcosis between 8 and 15 per cent., possibly at times more. One of the greatest features claimed for the apparatus shown is its simplicity; it represents a complete instrument for the following methods: gas alone, gas and ether, gas and oxygen, ether alone. The apparatus consisting of Fig. 1 was first devised for the administration of nitrous oxide gas alone. I then added the aseptic separable ether chamber for the gas-ether method (see *Journal of the American Medical Association*, December 15, 1900).

“The gas stop-cock (Fig. 1) contains two valves. The inspiratory valve is set in an inner cylindrical tube, which works by a handle through a right-angled slit in an external cylinder supporting the expiratory valve superiorly, and inferiorly giving attachment to the gas-bag for gas alone, or the inverted Y-shaped tube for gas and oxygen. The valves themselves are made of thin sheet hard rubber, and are therefore indestructible. When the handle is turned down to the point indicated by ‘air’ (see Fig. 1 diagrammatic plate, Fig. 4) the gas-bag is closed by means of the obturating function of the inner tube; when the handle is turned upward to the place indicated by ‘gas’ air is excluded and gas is inhaled by means of the inspiratory valve. Expirations of the patient pass out through the expiratory valve; at the same time the inspiratory valve is closed.

“When the handle is pushed backward to the place indicated by ‘no valves’ the valves are thrown out of action; the patient then breathes back and forth into the gas-bag. This three-way action of the stop-cock is a feature not represented in any of the dental gas inhalers of American manufacture.” This feature is used only with the gas and ether method.

The essential part of the gas and oxygen apparatus is an inverted Y-shaped tube (Fig. 2) attaching to the lower part of the valved stop-cock. It will be noticed that the right arm of the tubes is somewhat larger, to accommodate a revolving obturator which regulates the quantity of oxygen. This arm of

the tube is so constructed that when the obturator is fully open it represents exactly one-half that of the nitrous oxide arm; if so



Diagrammatic representation of stop-cock.

Dotted lines indicate external part of stop-cock, heavy lines and shaded part, internal tube. Arrows indicate direction of inspiration and expiration. The valves are indicated by shaded lines. A. Inspiratory valve. B. Expiratory valve. C. Index handle. D. Right-angled slit. P. Proximal end of stop-cock, attaching facepiece. X. Handle turned down; air breathed. X2. Handle turned up; gas breathed. X3. Handle turned up and back; gas breathed back and forth into gas-bag.

used it would represent exactly  $33\frac{1}{3}$  per cent. of oxygen. It may be said that anesthesia is never possible with such a large percentage of this gas. Graduations are accurately marked on

the surface of the tube as  $\frac{1}{2}$ ,  $\frac{1}{3}$ ,  $\frac{1}{4}$ ,  $\frac{1}{5}$ ,  $\frac{1}{10}$ ,  $\frac{1}{20}$ , representing, respectively, about 33, 25, 12, 6, and 3 per cent. of oxygen; these graduations have always reference to the *opposite* tube. The surface of the oxygen tube has also small depressions into which the metal spring slips when the oxygen is turned on; this permits the use of the apparatus without taking the attention of the administrator from the patient.

Fig. 3 shows the obturator, which opens by revolving from right to left. The small opening represents about 6 per cent. of oxygen. The vertical arm of the Y is the mixing-chamber for the two gases.

Two separate gas-bags are used, and by this means their respective distention may be more easily seen than with the single bag with septum. From four to six feet of rubber tubing connect the cylinders and gas-bags for transmission of the gases. The cylinders shown are the small portable ones of English manufacture, with foot attachment. Fig. 5 represents the gas and oxygen apparatus complete. There are two cylinders for nitrous oxide and one for oxygen, for the reason that a far greater quantity of nitrous oxide is used than of oxygen. The face-pieces of different sizes may be obtained of rubber, celluloid, or metal, with inflatable rims. For the cases having beards I have had made metal aseptic mouth-pieces of different sizes. These are used when for any reason atmospheric air cannot be entirely excluded. When using the mouth tube the nostrils must of course be closed.

In order to obtain perfect results with nitrous oxide and oxygen particular attention must be given to the following points:

The apparatus must be in perfect working order, and always tested by the administrator himself.

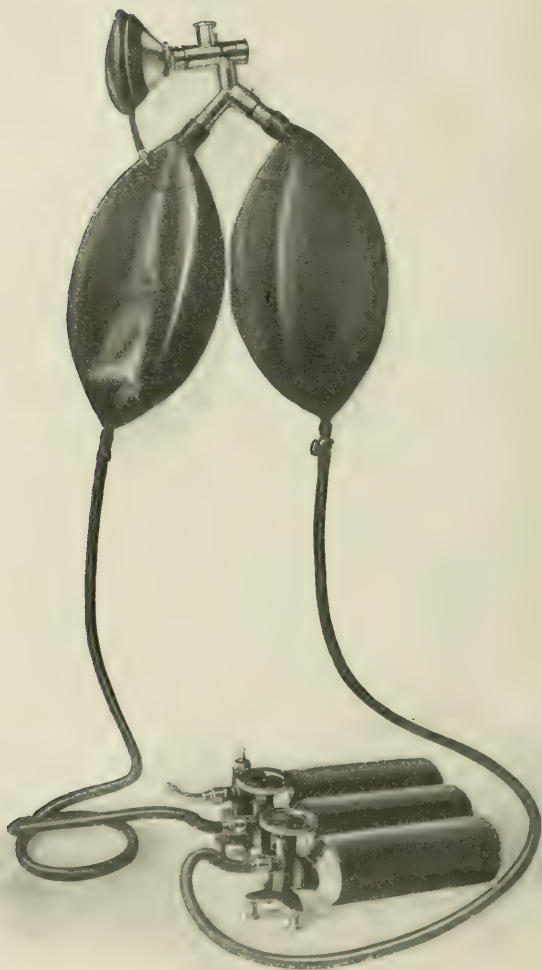
A sufficient supply of both gases at hand.

Atmospheric air must be rigidly excluded. In patients with beards, the nostrils may be closed; the mouth tube may be used instead of the face-piece, or the beard thoroughly moistened with water.

The patient should be prepared as for any other anæsthetic.

The gas-bags should never be fully inflated, but between one-half and two-thirds full. In this way the pressure of the gases is kept more nearly equal.

FIG. 5.



Oxygen should not be turned on immediately the administration begins, but sufficient nitrous oxide inhaled to replace the oxygen existing in the blood. Three to six breaths will usually suffice.

Oxygen should be admitted gradually, and in quantities determined entirely by the patient's condition, remembering cyanosis calls for more oxygen; evidences of excitement and returning consciousness meaning less oxygen is required. In using the gases in long narcosis the taps of particularly the nitrous oxide cylinders are apt to freeze, owing to the transition of the gas from the liquid to the gaseous state, the cylinders becoming covered with frost. To avoid this a towel wrung out of boiling water should be placed about the tap, but not about the cylinder itself.

The patient should always be placed upon the operating-table in the position in which the operation is to be performed. Any position may be employed providing it will not interfere with the administration of the anæsthetic. The preferable postures in my experience have been the dorsal or Sims.

Nitrous oxide and oxygen requires about double the time to produce its effect as does the gas alone, gas requiring from thirty to sixty seconds to induce anæsthesia; gas and oxygen from sixty to one hundred and twenty seconds. In either case consciousness is so quickly lost that I have found it generally impossible to obtain statements from patients as to their subjective symptoms. Sensations are pleasant or unpleasant, depending much on the temperament of the patient; hallucinations in some form are not infrequently experienced. As this may simply be a pleasant or unpleasant dream, it is occasionally difficult to convince the patients that they had not had an actual experience. I particularly remember a case where the patient, a man, upon recovering consciousness after gas for a short operation, for some time could not be convinced he had not been to a prize fight. It was amusing to hear his more expressive than elegant remarks regarding the affair.

When inhaling these gases the sensations are much the same as with gas alone. Anyone who has inhaled chloroform and nitrous oxide respectively must have noticed the similarity in the peculiar sweetish odor or taste. The oppressive sensations of gas

alone are usually absent, providing the gases are not inhaled from a long tube. I find these oppressive symptoms are more often due to the apparatus than to the gas, whether inhaled alone or in combination with oxygen. As the inhalation proceeds paræsthetic sensations are experienced in the tips of the toes and fingers and also the tongue. There is a more or less sensory anæsthesia while consciousness is still present. As the jaws become firmly closed it is well to insert a mouth-prop before beginning the administration, and also in oral cases when using the mouth tube instead of the face mask. Insensitive conjunctivæ and a snoring respiration are the best signs of anæsthesia. In dental cases this condition of snore should be permitted for from three to five minutes before removing the mask. It will then be found that the available operative period will be very appreciably longer than it is when using the gas alone. The color at the height of a gas oxygen narcosis is a pinkish hue, at times slightly bluish, but never the cyanosed condition as seen when using the gas alone. The pulse and respiration are approximately normal, somewhat more rapid if anything, and frequently far better than they were prior to the anæsthesia. The pupils are normal or moderately dilated, never markedly so; the lids are closed, the conjunctivæ insensitive. Perspiration is profuse, particularly in the longer narcoses. Relaxation in abdominal cases is not as profound as with ether or chloroform, and this, it may be said, is the only serious drawback to the use of this anæsthetic in abdominal work. Consciousness, even in long narcosis, is immediately regained.

It is evident that any agent capable of producing insensibility must have more or less shock associated with it. While this is true regarding gas and oxygen, this shock is infinitely less than with ether or chloroform. Convalescence is never delayed with this anæsthetic. Nausea and vomiting occasionally occur, particularly in the longer anæsthesias, but rarely persistent. Headache, more or less severe, is not an infrequent occurrence. Nitrous oxide and oxygen is the most expensive method of anæsthesia we have, owing to the large quantities of the gases used, depending upon the condition of health, type of the patient, and respiratory

activity. From a personal experience, I should say in an operation lasting one hour there would be consumed from 100 to 150 gallons of nitrous oxide and from ten to thirty gallons of oxygen.

In the report of the 100 narcoses where nitrous oxide and oxygen was used as the anæsthetic, I have selected those lasting half an hour and upward, the shorter cases covering almost the entire range of minor surgery, as tooth extractions, abscesses, curettings, etc., for a few minutes I have omitted. In the cases reported the operation in most instances was of shorter duration than the narcosis. When not indicated the anæsthesia continued from thirty to forty-five minutes.

1 case double amputation of the breasts and axillæ . . . . .	2 hours 40 min.
1 " single amputation of the breast and axilla . . . . .	2 " 0 "
1 " nephrectomy . . . . .	2 " 25 "
1 " exploratory cœliotomy for supposed tumor of the stomach . . . . .	1½ " 0 "
2 cases appendectomy . . . . . respectively 1½ hours and	1 hour 0 "
2 " abdominal hysterectomy . . . . . 1½ " " . . . . .	1 " 0 "
2 " removal of tubercular lymph nodes (see details of the third case where gas and oxygen was used) . . . . .	1½ and 1¼ hours.
1 case epicystotomy . . . . .	1 hour.
1 " cœliotomy ovarian cyst . . . . .	1 " "
2 cases perinephritic abscess . . . . . each	1 " "
1 case cœliotomy for abscess and removal of deep sutures . . . . .	1 " "
1 " removal of tumor from thigh and hemorrhoids . . . . .	1 " "
6 cases vaginal hysterectomy, two of these lasting 1 hour each, and one 2¼ hours.	
1 case prostatic hypertrophy (Bottin) . . . . .	
12 cases dilatation of sphincter and removal of hemorrhoids.	
1 case amputation of toes (for gangrene).	
3 cases posterior colpotomy.	
1 case anterior colpotomy and shortening round ligaments.	
2 cases cystoscopy (the position in one of these cases was the complete Trendelenburg, with thighs and legs flexed upon the abdomen).	
1 case excising rib.	
2 cases removal of axillary glands.	
1 case incising and packing mammary abscess.	
13 cases uterine curettage (simple).	
8 " " " (carcinoma).	
5 " " " (puerperal).	
1 case exploring, curetting, etc., sinus to kidney.	
1 " incising, packing, etc., parotid abscess.	
6 cases trachelorrhaphy.	
9 " perineorrhaphy.	
7 " trachelorrhaphy and perineorrhaphy combined.	
2 " varicocele.	
1 case abdominal wall abscess (typhoid).	
1 " catheterizing ureters.	

This case was anæsthetized by me for Dr. Howard Kelly, of Baltimore. The position—a most difficult one for any anæsthetic—was, first, the knee-chest for the placing of catheters, then the



dorsal for the taking of an X-ray photograph. The patient exhibited some muscular movements of the lower extremities, rendering this photographic feature impossible.

The details of the narcosis I had the pleasure of conducting for Dr. W. W. Keen in the Jefferson Medical College Hospital are as follows: The patient, a young lady, of anæmic type; pulse, respiration, and temperature normal. Anæsthesia was induced with gas and oxygen in two minutes, and maintained for thirty-three minutes. Consciousness was completely regained within one minute after the anæsthetic was discontinued. The color of the patient was a healthy pink, occasionally slightly blue. The blood was at times dark, but Dr. Keen said not more so than would occur with ether or chloroform. The pulse and respiration were about normal, pupil moderately dilated, eyelids closed at the beginning of the operation; the patient apparently once felt the knife. The operation consisted of the removal of adherent tubercular lymph nodes, during which the jugular was torn and ligated. Altogether, the narcosis was a most satisfactory one. I saw the patient about one hour afterward. She had vomited once; pulse the same as before operation; general condition good.

## DISCUSSION.

DR. JOHN D. THOMAS: I hardly feel competent to discuss the subject of nitrous oxide and oxygen, as it is one that I know practically so little about, my association with its use being almost entirely confined to dental operations. Nitrous oxide is undoubtedly the safest of all anæsthetics, for it has been used at the hands of operators of all grades of ability and experience, with the percentage of accidents almost nothing.

In former years there was a question as to whether the effects produced were from the want of oxidation or overoxidation. Certain it was that the appearance of the patient showed in some cases alarming conditions of asphyxia; but to-day it is accepted as a fact that nitrous oxide possesses strong anæsthetic properties; but, though composed of nitrogen and oxygen, the two are not separated at the temperature of the human body, consequently the gas is practically inert, and is accompanied with the asphyxiating appearances so painfully evident in many cases.

When the gas was first given it was nothing unusual to have to place a patient upon the floor and apply vigorous methods for resuscitation from

suspension of breathing, constriction of the glottis, or cardiac depression. These effects were more liable to occur in dental practice, for the reason that we had to place the patient in as profound a state of anæsthesia as possible to accomplish what was to be done in the mouth. For other operations, by carrying the patient just beyond the reflexes, the dangerous indications were not so frequent. It was in these cases, where the zone was sustained by alternating a breath of the gas with one of air, that it was noticed that the cyanotic exhibitions were greatly diminished, and from that we have come to always mitigating the asphyxia accompaniment by admitting air. So that to-day we never meet the dangerous symptoms which were formerly so common.

I was very much pleased with the exhibition given us to-day by Dr. Goldan. The patient was kept thoroughly anæsthetized for thirty-five minutes. There was considerable more cyanosis than I expected to see, and from experience we look upon rapid or marked discoloration as the sign of approaching danger, but from the fact that the patient actually was in no danger would prove that nitrous oxide is applicable to major operations.

DR. THOMAS R. BROWN, of Baltimore: I have listened with great interest to the paper by Dr. Goldan. During the past year I have employed the combined use of nitrous oxide and ether in Dr. Kelly's private hospital, where I have been in charge.

It has seemed rather strange to me that so little work in this direction has been done by practical men. The majority of the work has been done by the physiologists, to whom the subject has been one of great interest from the original observation of Sir Humphry Davy. His suggestions, however, were not given attention by surgeons, and the general belief has been that the anæsthetic was only feasible in dental operations. Subsequent work carried on by physiologists shows that its field of usefulness might be extended. Paul Bert's experiments are so well known that they hardly require mention here. His method, as we know, was to have the blood absorb a larger quantity of the nitrous oxide by raising the pressure, and thus producing anæsthesia without asphyxia. Martin showed that animals could be kept in this way under complete anæsthesia as long as three days, while Van Arsdale has worked along the same line. The great disadvantage of all these methods lay in the cumbersome and expensive apparatus employed, as it is only within a comparatively short time that the use of nitrous oxide and oxygen as an anæsthetic has been seriously considered, due to the invention of simpler methods and the discarding of the attempt to increase the atmospheric pressure.

My experience has been confined almost entirely to the use of nitrous oxide as a preliminary to ether, as I have had but fifteen or twenty cases of short anæsthesia by the nitrous oxide alone, all, however, perfectly satisfactory. The advantages of the combined anæsthetic (nitrous oxide and ether) are so numerous that I shall give them subsequently in detail. About

a year ago I became extremely interested in the subject of anaesthesia, as I was constantly being brought face to face with many of the discomforts that patients generally suffered, so that I felt everyone should be on the alert to discover some means of minimizing these factors so disturbing to convalescence. It was about this time that the literature of nitrous oxide came into the journals. I had been told that it had been administered by a well-known anesthetizer in the Massachusetts General Hospital, with disappointing results, while the only case which I had seen was one in which the cyanosis was so marked that I would not have suggested the use of the anæsthetic. I therefore took up the study of the use of the combined method in a far from optimistic mood. I afterward saw half a dozen cases in which it was administered in the service of Dr. McBurney, however, and was so favorably impressed that I have been using the method ever since. I think my views can be best expressed by quoting from an article which I contributed to the *Philadelphia Medical Journal* for November 3, 1900:

"One will see from this, therefore, that the method has proven of great value to us, and our experience in the one hundred or more cases anæsthetized since the appearance of this paper tends but to increase our faith: in fact, it has proven of such advantage to the patient in the rapidity of anæsthetization, the freedom from unpleasant symptoms during the process and the marked diminution in after-effects, as well as to the operator and the anesthetizer, that it has become an absolutely indispensable part of our operative technique."

DR. JOHN G. CLARK: Through the courtesy of Dr. Keen I saw Dr. Goldan anæsthetize a number of cases to-day in the Jefferson Surgical Clinic, and I was very much pleased with the action of the anæsthetic both in the rapidity of the administration and in the maintenance of uniform narcosis throughout the operation.

In the first case, in which nitrous oxide alone was used, the patient was under the anæsthetic in less than three quarters of a minute, and the operation was begun.

In the second case, in which nitrous oxide and oxygen were given in combination, the operation was under way in less than three minutes from the time the cone was placed over the face.

While I can see very little to criticise in the administration of these various anæsthetics, for they were most successfully given by Dr. Goldan, I was, nevertheless, impressed with one fact, and that is, that only in the hands of a skilled anesthetizer would they be entirely safe.

While visiting the London hospitals recently, I was impressed with two facts: First, that the surgery is not equal to that of our country, and second, that the anæsthetics are uniformly given better than in this country. This is due to the fact that an official anesthetizer is attached to each large clinic, whose sole and only duty is to give the anæsthetics—not for three

months, as we have it in our rotation interne service in this country, but for years. In fact, in one clinic the anesthetizer told me that he had acted in that capacity for twenty years. The advantages of this course are obvious, for we know that as a man gains experience in the administration of ether and chloroform the immediate dangers and subsequent ill effects largely disappear. From these remarks it may be gathered that the criticism which I would offer at this time is not with the method of administration as practised by Dr. Goldan—which is not to be criticised, but highly commended—but the rotation service in our different Philadelphia hospitals would prevent the anesthetizer becoming sufficiently skilled in his short service to justify its employment. If it is possible to have an official clinic anesthetizer, then the administration of anesthetics according to the various plans suggested by Dr. Goldan is certainly advisable. Dr. Goldan deserves our congratulations for having so thoroughly worked out and demonstrated the practicability of his methods.

One query has come up in my mind in connection with this method of administering anesthetics which has been answered by Dr. Brown in his discussion, and that is as to whether the severe bronchorrhœa, which is so troublesome at times when ether is given, is eliminated by this method. From what Dr. Brown has said the same difficulty is observed by the novice with his newer method.

The one further difficulty which would, unquestionably, stand in the way of the general adoption of this method for the clinics in eleemosynary institutions is the expense. For instance, I was told to-day by a gentleman who was present at Dr. Keen's clinic, that the amount of oxygen and nitrous oxide used during his clinic would cost about \$10. This expense would, therefore, prove a very serious obstacle to its general adoption.

DR. W. W. KEEN: Dr. Goldan kindly administered the anæsthetic at my clinic to-day to two patients. The first was a child in which I had to remove a nævus from the upper lip. It was a very unfavorable case, and for that very reason I chose it because it gave me an opportunity to test the method under great difficulties. The child was not completely anesthetized all the time, but satisfactorily so as far as the surgeon was concerned.

In the second case anæsthesia was complete in two and a quarter minutes, and the operation lasted thirty-three minutes. I removed two glands from the neck, one of which was adherent to the jugular vein. In one minute from the time the anæsthetic was discontinued the consciousness of the patient had entirely returned and without any untoward symptoms afterward. I was much pleased with the result, especially with the fact that during most of the time the countenance was of the ordinary pink hue. There was occasionally a little of the cyanosis that one sees in the administration of nitrous oxide alone, but additional oxygen quickly restored the color.

DR. GOLDAN (closing): Regarding the use of nitrous oxide before ether, it is surprising that it should not be used more generally. The advantages of the method over ether alone are its safety, economy, rapidity in inducing anaesthesia (from two to four minutes) lessened anaesthetic shock; greater rapidity in return of consciousness and more rapid convalescence. The method is not difficult to learn, the apparatus quite simple. The two apparatuses shown were devised by myself, the first is made without valves, in which the patient breathes back and forth into the gas-bag; after being anaesthetized with gas the wire basket with gauze saturated with ether is quickly inserted; the patient then breathes gas and ether; during the transition the patient will occasionally hold his breath, due to the strong ether vapor—this lasts but a moment, and the patient passes into deep ether anaesthesia, averaging, in my experience, three minutes. This apparatus is the simplest ever devised for this method of anaesthesia. The other apparatus is made with valves whereby the transition from gas to ether is very gradual. While the gas and oxygen method of anaesthesia requires more skill to administer, there is no reason why the method should not be taught in all hospitals—internes are taught to be surgeons but not anaesthetists. A good plan, it seems to me, would be to have in each hospital the same number of anaesthetists as there are surgeons. In this way there could then be in attendance each day a skilled administrator supervising the work of the interne throughout his entire term of service.

# A NEW CLASSIFICATION OF THE DISEASES OF THE BONES AND JOINTS.

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[Read April 3, 1901.]

FOR some years past my attention has been called from time to time to the lack of classification of the diseases of the bones and joints in the text-books upon these subjects. Most of the classifications which are in use date back to the time of Brodie. Many text-books upon surgery do not give any classification. The greater attention given to pathology of late years has greatly advanced the knowledge of these subjects.

In preparing this classification all the available works upon surgery and pathology have been consulted.

The classification is clinical, and is based upon the pathology of the structures involved. The first column contains the seat or structure involved, the second the pathological processes, and the third the diseases according to their Latin or English names. The last two columns deal with the variety of the disease and the synonyms.

The author has found it useful in the study of these subjects, and presents it with the hope that its usefulness may be extended.

My best thanks are due to Dr. George Robinson for clinical and clerical assistance in the preparation of the work.

## A CLASSIFICATION OF BONE DISEASES.

Seat.	Process.	Disease.	Varieties.	Synonyms.
Nerves	Atrophic		Neuroparalytic Neuropathic	
Vessels		Aneurism Thrombosis Embolism Rickets		
	Inflammatory	Laceration Abscess	Acute hematogenous Metastatic	
	Inflammatory	Periostitis	P. ossificans P. spongoid P. fibrosa P. acute infective	P. purulenta maligna
	Infect. granulomata		P. tuberculosa P. gummosa	
Periosteum		Osteomata	Compact Spongy Medullary	O. durum O. spongoid O. medullare
	Tumorous: Primary	Exostoses  Fibromata Chondromata Myxomata Sarcoma	Fibrinous Cartilaginous  Osteofibromata Osteochondroma Myxofibroma All varieties	Ossifying osteoma Osteomyxoma
	Secondary	Sarcoma Carcinoma Fatty degeneration Necrotic foci Siderosis Hemorrhagic		Hypertrophy of fat
	Degenerative			
	Inflammatory	Osteomyelitis	Acute infect. O. O. fibrosa	
		Osteoma Myxoma Fibroma Chondroma Sarcoma	Enostoses Myxofibroma	Osteomyxoma
Medulla	Tumorous: Primary		Osteochondroma Intraosseous epulis Alveolar S. Myeloma Angioma Osteosarcoma Chondro-S. " osteosarcoma	Endothelioma Telangiectatic S. Ossifying S.
	Secondary	Sarcoma Carcinoma.		
			Eccentric Concentric Senile	Symptomatic osteopsathyrosis Fragilitas ossium
Osseous	Atrophic		From disease " pressure Erosions Osteoporosis Caries Necrosis Necrotic caries Halisteresis ossium Osteomalacia	



A CLASSIFICATION OF BONE DISEASES—*Continued.*

Seat	Process.	Disease.	Varieties.	Synonyms.
Osseous	Hypertrophic		Callus Hyperostoses Synostoses Syndesmoses Osteophytes Osteosclerosis Periostoses	
			O. deformans Osteomyelitis ossificans O. ossificans genuaunt O. rarefying Osteochondritis Hypertrophic O.	O. hypertrophica Acromegaly Marie Pachyacia (von Recklinghausen) Pulmonary hypertrophic osteoarthritis
	Inflammatory	Ostitis		
	Infect. granulomata		Tubercular Syphilitic Actinomycotic Leprosy glanders } rare	
	Faulty growth		Agensis	Osteogenesis im- perfecta Nagashima
			Microsomia Chondrodystrophy hypoplastica Chondrodystrophy hyperplastica	Achondroplasia
	(Intrauterine)		Chondrodystrophy malacia Premature synos- toses	Micromelia chondromalacia
	(Overgrowth)	Separation of epiphyses.	Gigantism	Leontiasis ossea
	Tumorous: Primary	Osteoma Chondroma	Osteochondroma	
		Sarcoma	All varieties.	
	Secondary	Cysts	Hydatid Disintegration (degen. of tumors)	
		Sarcoma Carcinoma (most common)	All varieties Nodose Diffuse C. osteomalacia C. caries	

## DISEASES OF JOINTS.

Seat.	Process	Disease.	Variety.	Synonyms.
Nerves	Inflammatory	Neuritis Paralysis Neuropathic A.	Articular neuralgia Tabes dorsalis	Hysterical joints Charcot's joint Spinal arthropathies
		Impaired nutrition	Rickets, scurvy, gout Elephantiasis, syphilis	Chronic gouty A. S. epiphysitis S. gumma
Vessels	Infectious	Rheumatism	Ac. rheumatic A Chronic " A. Multiple arthritis	C. ankylosing A. Schönlein's disease
		Peliosis rheumatica Septic A.	Ac. infantile A. Gonorrhoeal A. Typhoid A. Acute epiphysitis	
Periarthritic structures	Trauma	Hemorrhage		
	All tissues	Periarthritis		
	Bursa	Adventitious burse Bursitis Sloughing B. Hygroma Enlargement of B. Traumatism	Solid Wounds	Dropsy of B.
	Capsule	Capsulitis Arthritis deformans Extra cap. ankylosis		Rheumatoid A.
	Tendon	Tenitis thecitis Tenosynovitis Rupture Dislocation Lipoma		
	Extra cap. ligaments	Sprain, rupture Relaxation Laceration		
	Inflammatory	Periostitis osteitis Ac. osteomyelitis Bony ankylosis		
	Osseous tissue	Traumatic	Dislocation	Partial, complete Consecutive Congenital
Fracture involving joint				
Tumorous		Enchondroma Exostoses Osteophytes Sarcoma Carcinoma		

DISEASES OF JOINTS—*Continued.*

Seat.	Process	Disease	Variety.	Synonyms.		
Arthritic structures	Synovial membrane	Inflammatory	Synovitis	Acute serous S.	Acute articular dropsy	
				Chronic serous S.	Chronic articular dropsy	
				Purulent S.	Pyarthrosis	
				Tubercular S.	Arthropyrrosis	
					Empyema of joint	
					Tubercular A.	
	Tumorous				Fungous A.	
					Granulative A.	
					Hydrops tubercular	
					Tubercular empyema	
					Tumor albus or white swelling	
	Cartilage				Neures articuli	
						Fibrous interosseous ankylosis
						Cysts
						Ganglion
						Simple synovial
Adventitious						
Simple						
Compound						
Epiphysitis						
Caries erosion						
Necrosis						
Cartilaginous ankylosis						
Sequestra						
Loose bodies						
Int. artic. ligaments						
					Relaxation	
					Laceration	
All tissues						
					Rupture	
		Panarthrititis				

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HYDROCELE: ITS TREATMENT: SUMMARY OF 338  
OPERATIONS; DESCRIPTION OF NEW METHOD  
SUGGESTED BY DOYEN FOR THE RADICAL  
CURE OF HYDROCELE OF THE TUNICA  
VAGINALIS TESTIS.

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AFTER having investigated the literature of hydrocele the surgeon will be astonished to find how many methods of treatment have been suggested for the radical cure of the disease. Want of space and time will prevent my doing more than taking up for consideration those methods only which are in vogue at the present time, and have proved to be of value. That chronic hydrocele is rebellious to treatment is patent to anyone who has had much experience with the disease: this, too, is shown by the extraordinary number of expedients which have been recommended for its relief. At the present time there are five different methods of treatment employed with a view to effecting a radical cure. They are: (1) Acupuncture (for infantile hydrocele); (2) tapping and injecting with irritating substances; (3) antiseptic incision; (4) incision, with partial excision of the sac; (5) incision, with inversion of the tunica vaginalis testis.

Cases where spontaneous cure has unexpectedly taken place have been occasionally observed; notably by Terrillon and M. M. Monod. I have had a similar experience with a patient who was referred to me several years ago by Dr. Joseph Price, of this city. The individual had an ordinary hydrocele of the left side containing about

eight fluidounces; it had made its appearance one year before I first saw the case. I suggested a radical operation, to which the patient consented, but stated that business affairs made it necessary for him to postpone surgical interference for at least three months. Soon after, to my surprise, the tumor began gradually to diminish, and at the end of a month it had completely disappeared. A spontaneous cure may be looked for in some instances where there has been an inflammatory condition of the scrotum following traumatism, epididymitis, orchitis, or erysipelas. A case is reported where absorption of the fluid took place after a sharp attack of gout and another after recovery from smallpox. This fortunate and much to be desired result is unfortunately so rare as not to be regarded as one of the probable terminations of the malady.

I am indebted to one of my clinical assistants, Dr. Henry Tucker, for arranging the following table from my operating-book of the genito-urinary department of the Jefferson Medical College Hospital. The table gives the number and character of cases operated upon from 1894 to 1901:

Hydrocele congenital (resection and ligation of funicularform process) . . . . .	2
Hydrocele, diffused of cord . . . . .	2
" double (resection of both sacs) . . . . .	19
" ("en bassac") . . . . .	1
" encysted of cord (resection of sac) . . . . .	17
" " " with hernia (radical cure of both) . . . . .	1
" " of epididymis (resection of sac) . . . . .	7
" " of tunica albuginea . . . . .	5
" (spermatic cyst) . . . . .	1
" infantile (antiseptic incision) . . . . .	9
" (needle operation) . . . . .	25
" inguinal (castration and resection of sac) . . . . .	3
" " complicated with hernia (castration, resection of sac and radical cure of hernia) . . . . .	4
Hydrocele (resection of sac, transplantation of misplaced testicle and radical cure of hernia) . . . . .	2
Hydrocele multilocular . . . . .	1
" obliterated hernial sac . . . . .	2
" tunica vaginalis (antiseptic incision) . . . . .	25
" " " (double antiseptic incision, both sacs) . . . . .	8

Hydrocele	tunica vaginalis and encysted of cord	. . . . .	8
"	"	" inguinal hernia (radical cure of both) . . . . .	9
Hydrocele	tunica vaginalis (resection of sac)	. . . . .	94
"	"	" inversion of tunic . . . . .	8
"	"	" (tapping, palliative operation)	84
"	"	" with encysted hydrocele of epidi- dymis . . . . .	1

On consulting this table it will be seen that 338 operations were performed for the relief of the various known forms of hydrocele, some of which were very rare and of unusual interest. No deaths resulted from any of the operations. The cases treated included all ages from infants a few weeks old up to septuagenarians. This would seem to show that with proper antiseptic precautions the dangers attending the various methods of operation for hydrocele are slight. The patients who were treated by the method known as "antiseptic incision" usually left the hospital on the sixth day, while those whose sac was partially resected were able to leave the institution on the ninth day.

Thirty-four of the cases were infants who were operated upon by the method known as the "needle operation," or "acupuncture." Of this number nine cases recurred and were again operated upon, antiseptic incision being employed in the second instance. In two out of the nine cases so treated recurrence took place, and in each instance the sac had to be partially resected before a cure was effected. Thirty-four adults were operated upon by the method known as "antiseptic incision," of which number the hydrocele was double in eight cases. So far as we have any record, recurrence took place in nine cases, rendering another operation necessary. Partial resection of the sac was performed in ninety-four cases; in two instances the hydrocele being double, both sides were operated upon at the same time. Recurrence has been known to take place in but one case. In performing the needle operation in infants it was found that acupuncture had to be performed from four to six times at intervals of once a week until a cure was secured. The antiseptic incision was reserved for diminutive cases, where the sacs were thin, and had not been tapped or injected with irritating substances, the sac being

limited to the scrotum and not extending up into the inguinal canal. For the past two years this operation has been performed by cocaine infiltration anaesthesia, a 1 per cent. solution being employed. Out of the number operated upon, recurrence took place in nine cases. The number of cases in which relapses occurred is possibly larger than that named, as it is probable if recurrence did take place the individuals were either in different parts of the country or had sought relief elsewhere. From the results obtained from this operation, while it is safe and easily performed, it does not appear to be very reliable. Its usefulness seems to be limited to small recent hydroceles, with thin sacs, which have been neither tapped nor injected. Tapping or injecting with either iodine or carbolic acid had been performed in six of the cases which have been reported previous to making the antiseptic incision, and even after the latter operation had been accomplished four of the cases so treated recurred. This operation was employed by me before I had an extended experience with the radical treatment of hydrocele. In later years I have partially resected the sac in wellnigh every instance.

The cases selected for partial excision of the sac were those where the amount of fluid was large; which had extended upward into the inguinal canal, and which had been previously treated by means of injection of irritating substances. The mode of operating employed differed somewhat from that recommended in the text-books. An incision was made over the tumor dividing the tissues down to the sac, taking care not to open the tunica vaginalis, which was dissected entirely free from the adjacent textures and brought out through the incision in the skin. The sac was then opened throughout its entire length and trimmed away with scissors; the portion covering the cord was mopped off with pure carbolic acid. If hemorrhage from the cut margin of the sac proved troublesome it was controlled by means of a continuous catgut suture applied along both edges of the divided tunic. The wound was then closed in the usual manner and a small quantity of iodoform gauze was left in the dependent portion of the incision for the purpose of drainage; this was removed at the end of twenty-four hours.

The method of treatment here described has proved most satisfactory. As far as is known recurrence has taken place in but one



instance. Return is less liable to take place after this operation than after any other hitherto suggested. It is the most extensive and severe of any of the methods that have been employed up to this time; hemorrhage is sometimes troublesome if the sac is very thick and has been repeatedly tapped, or if it has been injected with carbolic acid. Out of the ninety-four cases so treated fifteen cases had been repeatedly tapped and eighteen had submitted to the injection of stimulating substances resulting unsuccessfully. In eighty-four cases the palliative treatment was employed. This consists in simply evacuating the fluid contents of the sac by means of a trocar and canula, or by the use of an aspirating needle. This method of treatment was reserved for patients who were very far advanced in years or suffered from some chronic disease of the heart, lungs, or kidney. For the purpose of tapping a hydrocele most surgeons employ a trocar and canula designed for the purpose. I have found that an aspirating needle about the circumference, No. 9 M., French scale, is preferable, as the sight of a small needle gives rise to less fear in timid individuals than does that of the trocar; it is inserted with less pain and the wound inflicted in the scrotal tissue is much smaller, and consequently there is less danger of infection. I have employed both instruments in numerous cases and have found the needle to be the more satisfactory.

It will be observed that none of the cases reported were treated by tapping and injecting irritating substances into the sac. The late Professor S. D. Gross advocated the use of tincture of iodine as an injection, and Dr. R. J. Levis was the first to suggest the employment of carbolic acid; as clinical assistant to both these gentlemen, I had abundant opportunity to witness the results obtained from the use of these fluids. In the majority of the cases when the tincture of iodine was employed the termination was extremely unsatisfactory. Its use was usually attended by a prolonged convalescence, the patient often being confined to his bed from ten to fifteen days; in many cases two or three months elapsed before the surgeon knew definitely whether or not a cure would be effected. Immediately after the injection of either tincture of iodine or carbolic acid the sac became enormously distended and was usually attended with a great deal of pain. In many cases relapses occurred. Jacobson

states that "in twenty-five cases so treated at St. Thomas' Hospital recurrence took place in eighteen." Of nineteen cases treated by Bardeleben but 65 per cent. were cured. Jacobson estimates the recurrence in our climate from this method of treatment to be about 10 per cent. In my experience this is rather a low estimate. Extensive œdema of the scrotal tissues has been reported following the escape of either tincture of iodine or carbolic acid into the structures. Suppuration of the sac, abscess of the testicles, and carbolic acid poisoning have all been noted. In one case treated by means of carbolic acid injection, abscess of the testicle followed, involving the cord, giving rise to a lymphangitis; death finally taking place from sepsis.

The only thing which commends tapping and injecting a hydrocele sac is the fact that it is readily and rapidly performed. The objections to tapping and injecting for hydrocele are so numerous that most surgeons now resort to the open operation, it being by far safer and less painful, with quicker convalescence and a diminished liability to recurrence.

It will be observed that the treatment employed in the cases here recounted was not entirely satisfactory. The method which uniformly gave the best results was when the sac was partially resected. This operation required an anæsthetic, took some time to perform, the operation frequently being prolonged in order to give attention to controlling the annoying hemorrhage that supervened. About nine days were required for convalescence, after which there was no certainty that a recurrence would not take place. The profession is therefore still in a position to adopt with cordiality any new method of treating this affection that will take less time in its performance; that will be attended with less pain and be followed by a greater certainty of a radical cure. It is believed that an operation which fulfils these indications has at last been devised and is so simple that the wonder is that it had not been thought of before.

In 1898 Winkelmann published in the *Centralblatt für Chirurgie* (No. 44, p. 1092) a description of a new method of operating on ordinary chronic hydroceles, which seems to answer all requirements and solve the vexed question as to what may be the most practicable. The operation is performed under local anæsthesia, Schleich's infil-

tration method being employed. The ordinary incision is made through the scrotal tissue until the tunica vaginalis is reached. An opening is then made in the upper portion of the sac in the vicinity of the cord large enough to permit the testicle to be drawn through, after the fluid is evacuated, when the tunica vaginalis propria is turned back or everted. In order to prevent the testicle from slipping back into the sac the upper portion of the tunica vaginalis is secured by means of fine catgut to the fascia of the cord, a suture being at the same time placed at the lower end of the repleted tunica, thereby anchoring the tunic in its new position and preventing the testicle from returning to its normal position. The testicle together with the inverted sac is then replaced within the scrotum and the wound closed by means of a couple of interrupted sutures. The time employed for the operation is less than ten minutes. As it is not attended by hemorrhage no ligatures are needed.

When studying the subject of hydrocele I found that a precisely similar operation to that of Winkelman had been previously described by E. Doyen, of Reims, France, in the *Archives Provinciales de Chirurgie* (1895, Tome iv., No. 2, p. 706), under the title of "Radical Cure of Hydrocele by Inversion of the Tunica Vaginalis," thus antedating the publication of Winkelman by three years, so that it appears the credit of first suggesting this process belongs to Doyen and should receive his name.

I am under the impression that this operation was first performed in this country by Professor W. W. Keen at the surgical clinic at the Jefferson Hospital on January 16th of the current year. In the minutes of the case it is noted that: "The operation required less than ten minutes to perform. No ligature was required. The highest temperature reached was 99.2°. The patient left the institution on the twelfth day, cured."

Since witnessing the operation here referred to, I have had the opportunity of performing it eight times. My experience in each instance has been similar to that of Dr. Keen. The largest hydrocele contained one and a half pint of fluid. In each case the time required for the performance of the operation was about nine minutes. No ligature was required and the patients were enabled to leave the hospital on the ninth day.

In large hydroceles of long standing, with greatly thickened sacs, the operation would not be feasible and the partial resection of the tunic would have to be resorted to. This is illustrated by a case that came under my care one week ago. The individual was a mounted policeman, who stated that two years ago he struck his scrotum against the pommel of his saddle and in consequence a hydrocele was developed: that two weeks before presenting himself at the hospital he had knocked the tumor violently against the corner of an ash-box, when it became very much enlarged and painful and at the same time turned "as black as his shoe." On opening the sac a pint and a half of serum mixed with blood and bloody clot was evacuated. The sac was thickened to the extent of about one-quarter of an inch, and it was firmly adherent to the surrounding tissues. It was dissected loose with difficulty. The thickness of the tunica in this instance would have rendered inversion an impossibility. It is interesting to note that the cause of the hæmatocele was found to be due to a rupture of the tunica vaginalis propria about two and a half inches in length at the bottom of the sac, directly opposite the point at which the blow had been inflicted.

In all the cases operated upon by inversion of the tunica vaginalis a painless enlargement of the testicle resulted: it was, however, not attended with any rise of temperature, and it gradually subsided in about ten days. This condition is precisely similar to that which always follows the open operation for hydrocele. The first case operated upon by me, on January 18th last, was seen two days ago.

The individual was perfectly well and a trace of the operation was detected only by making a careful examination.

This new operation is still on trial. My experience is too recent for me to determine whether a recurrence of the ailment may or may not take place in any of the cases that have been under my supervision. From the fact that the inverted tunica vaginalis must become attached to the surrounding structures and the cavity formed by this sac is thus permanently obliterated it would look as if a recurrence of the condition would be an impossibility. The removal of the entire tunica vaginalis, except a small strip covering the cord, in ninety-four cases has convinced me that no fear need be enter-

tained as to the result of injury to the testicle by being deprived of its natural covering.

My limited experience with this new method of treatment inclines me to the belief that it will prove to be the most satisfactory operation which has as yet been suggested for the radical cure of an ordinary chronic hydrocele.

## PRE-EXISTING HEART DISEASE IN REFERENCE TO SURGICAL OPERATIONS.

By WILLIAM J. MAYO, A.M., M.D.,

ROCHESTER, MINN.

[Read by invitation May 1, 1901.]

THE demands of modern life tax the energies of the individual to the utmost. A sound heart in a sound body acquires a new significance, for the stress falls to a large extent upon the circulation. Clinical observers of wide experience believe that diseases of the heart are on the increase, not the mechanical lesions which we so long considered the chief source of cardiac disability, but failure of the heart muscle through disease.

We have, heretofore, measured the heart power by the size of the obstacle to be overcome, but in reality more depends upon the perfection of the cardiac contraction and its ability to overcome resistance. The normal heart has a vast reserve power. The sound muscle fibre quickly recuperates from overwork, and the circulation but momentarily fails. This is not true of the compensating heart. Hypertrophy is a conservative process, but it does not begin at the exact moment the circulation is obstructed, but at a time when at least a portion of the reserve has been expended. Compensation in itself presupposes a lessened reserve force. The more exactly the compensation balances the obstruction the less the liability of cardiac failure under temporary stress. To the surgeon the condition of the cardiac muscle is of prime importance. A crippled heart may compensate for the ordinary affairs of life, but the question is, has it sufficient reserve force to carry on its function during an operation, which, though temporary in character, is attended by an increased call upon the heart's strength? The dangers to be feared are very real, and do not lie entirely in the anæsthetic. The necessary injury to the nerves and other tissues of the

body with the loss of blood must be taken into account, and the amount of this operative traumatism cannot always be foretold with certainty.

The circulation demands that the arteries be kept overfull; the heart must be equal to keeping the pressure in the arteries greater than in the veins, and premonitory symptoms of a failing compensation must be earnestly sought before an operation is undertaken in the face of cardiac disease. The reserve power of the normal heart is not as great in infancy and old age, although the writer has not found this to be as true of the latter as the former period of life. Very fleshy people have less reserve force, and from an operative stand-point are generally looked upon with suspicion. People of unusual height are also supposed to have relatively less cardiac reserve. Our experience in the Northwest with people above the average height has been considerable, and we have found them, as a rule, most excellent subjects for operation.

The enervation of the heart plays an important part in estimating an operative risk. It must, at least, be sufficient to enable the reserve force to be called into play. It is demonstrated that the power of contraction lies in the muscle fibre of the heart itself, and exists before the cardiac plexus is formed. The vagus and sympathetic are integral factors in the cardiac ganglia, and disturbance of function resulting in excessive rapidity or slowness of the cardiac pulsations may often be traced to reflex conditions acting through the nerve-supply or be a personal or family idiosyncrasy. An irregular or intermittent pulse may also result from the abuse of tea, coffee, or tobacco. The cause in any event should be determined, and the probable influence upon the patient's ability to withstand an operation estimated.

Heart lesions may properly be divided into two general classes: First, valvular and endocardial disease; second, myocardial changes. The sharp distinctions between them have, however, passed away with the advent of better knowledge of the subject. Myocardial changes are often found associated with valvular disease, particularly so when compensation begins to fail, while in the latter stages of myocarditis secondary valvular lesions are common.

Between the ages of ten and forty valvular disease is usually well compensated, and if the heart's action is easy and the circulation well carried out the operative risk is not great, and in our experience we have never lost a patient from this cause. There is but little liability of overlooking the condition, the early development of characteristic murmurs and the ease with which the hypertrophy can be recognized enables the surgeon to gauge the disability with a fair degree of



accuracy. The operation is undertaken with full knowledge of the cardiac disability and its character, and the choice of an anæsthetic is greatly influenced by this condition. If there is failing compensation and signs of marked dilatation only operations of the greatest urgency would be undertaken without preparatory treatment. It is fortunate that valvular lesions are the most common during the active period of life, at which time the large majority of operations becomes necessary. After forty, valvular lesions are usually associated with some degree of myocarditis.

I do not wish to be understood as minimizing the importance of primary valvular lesions, but rather to point out that the ease of diagnosis and the fair degree of accuracy with which the compensation can be estimated does not render it a frequent cause of operative mortality. The knowledge of the cardiac insufficiency robs it of much of its danger.

Myocarditis is the condition which the surgeon has reason to fear. There are often no sign-posts of danger, and the first intimation of trouble is the sudden death of the patient upon the operating table or shortly afterward. It may happen that the operation was performed for the relief of some condition which in itself was not serious, and which would not have been undertaken if knowledge of the heart disability had been previously obtained.

That a heart which is not increased in quantity as estimated by the usual means of diagnosis and the quality of its action seemingly unimpaired should suddenly fail when called upon for a temporary reserve force, is an appalling fact, but nevertheless true. Fortunately, the large majority of cases do give signs and symptoms which if looked for with care will enable the surgeon to detect the possibility of disease, and in the later stages the diagnosis may be self-evident. Cardiac symptoms after middle life not plainly pointing to valvular lesions are probably myocardial in origin. Preble quotes the following on myocardial disease from Huchard: "Their evolution is latent, their beginnings insidious, their course paroxysmal, their progress interrupted. They are complicated by a variety of visceral manifestations, and are brutally sudden in their explosions of cardiac insufficiency."

Acute myocarditis results from various infections and may date its origin to an attack of diphtheria, gonorrhea, quinsy, influenza, or other infectious disease. If death occurs primarily there may be no macroscopical evidence of disease of the heart, the changes are microscopical (Stengel). Acute myocarditis usually passes into the chronic form, but the large majority of cases of chronic myocarditis are so from their



inception. The disease is marked by the development of fibrous tissue, and other nutritive changes brought about through lesions of the coronary arteries. Rosenbach believes the fibrosis to be a conservative process and that it braces up a feeble muscular power. Freer, on the contrary, maintains that it is primarily a destructive one, and analogous to fibrosis of the kidney.

Fatty degeneration of the heart, according to Strümpell, Van Leyden and others, seldom gives signs of its presence excepting in the later stages.

In experimental fatty degeneration produced by Hasenfeld and Fennyvessy, there was no change in the cardiac size nor was the rhythm or force of the pulse affected. Stokes considered pseudo-apoplexy, soft blowing systolic murmurs with a slow pulse, pathognomonic of fatty degeneration, but as myocarditis was but little understood in his day it was only the cases in which this condition was more marked than the fibroid changes which were recognized. Fatty degeneration is often an accompaniment of myocarditis or one of its results, and the great loss of reserve force which it produces, together with the difficulty of even an approximate diagnosis, makes it the most serious disease of the heart from a surgical stand-point.

Lesions of the aortic opening and valves appearing about middle life can also be classed with myocarditis, and are often associated with it. Changes in the coronary vessels and at the base of the aorta usually coexist. This form of valvular disease has what may be called a physiological basis, and is more serious than similar lesions at the aortic opening in the young. Benike, by a series of measurements, has shown that after forty the aortic opening gradually increased in size, and it is easy to understand how severe work or disease might lead to grave consequences. Myocardial changes, associated with arterio-sclerosis and contracted kidney, must also be taken into account.

The writer does not wish to discuss the symptomatology nor pathology of myocarditis, but merely to call attention to the diminished reserve force of the heart which it entails, and point out that many of the unexpected and sudden deaths which take place at or soon after an operation are due to this cause. A patient in middle or later life showing signs of progressive cardiac weakness manifested by a vigorous heart contraction with a feeble pulse, irregular in rhythm and associated with cardiac pain and attacks of dyspnoea with general loss of strength, is to be looked upon with suspicion, and an operation is not to be slightly undertaken. The more advanced cases of myocardial

disease present such characteristic symptoms that only life-saving procedures would be indicated. Illustrating the operative mortality, the two following cases are briefly reported.

*CASE I. Cholecystotomy in patient with chronic myocarditis; sudden death forty-eight hours after operation.*—Mrs. J. D., aged thirty-five years, American. First came under observation in September, 1900, with a history of gallstone disease. On examination the heart's action was found to be 120, pulse feeble and intermittent, a faint mitral murmur could be detected. There was slight increase in size. Patient complained of attacks of dyspnoea and oppression in the chest, and at times slight vertigo. No direct history as to the origin of the cardiac lesion. The attacks of colic were frequent and very distressing. Patient pale and anæmic. In the face of grave myocardial disease operation was not advised at this time. On January 5, 1901, she was readmitted to St. Mary's Hospital; the heart's action was very much improved, pulse 112, fairly good quality. Patient's physical condition better, but the attacks of gallstone colic were frequent and some jaundice had followed the last attack. On January 8th cholecystotomy was performed. The operation was easy and quick. There were no complications. Anæsthesia, nitrous oxide, and ether. Time, twenty minutes. Patient was in excellent condition for forty-eight hours, when she suddenly died from cardiac failure without premonitory symptoms.

*CASE II. Abdominal hysterectomy for malignant disease in patient with chronic myocarditis; death on operating table from chloroform anæsthesia.*—Mrs. E. E., aged forty-eight years, German. Admitted to St. Mary's Hospital on January 10, 1901. This patient came under observation four years ago with an ovarian tumor, and at that time had physical evidences of myocarditis. The tumor was removed under ether anæsthesia. She had remained in fair health except for occasional attacks of dyspnoea, palpitation, and a chronic cough. She returns now for the relief of malignant disease of the body of the uterus. On the day following admission the patient developed influenza and bronchial pneumonia, and over two weeks elapsed before she was in a condition for operation. The heart's action was forcible, the pulse full, intermittent, and 120 to the minute. There was marked hypertrophy and a mitral murmur, with evidence of chronic myocarditis. On January 26th abdominal hysterectomy was undertaken under chloroform anæsthesia. This anæsthetic was chosen on account of the bronchitis which had been much aggravated by recent illness. The patient took the anæsthetic badly, and was given but little. The operation had pro-

ceeded about ten minutes, when the heart's action and respiration suddenly stopped and the patient could not be resuscitated.

Heart lesions secondary to the disease for which the operation is undertaken may be either valvular or myocardial, usually the latter. The most common are due to obstructed circulation by the pressure of large tumors, especially uterine myofibromata. Hofmeier collected eighteen cases in which sudden death occurred from this cause. Williams, of Bristol, in eight fatal cases unoperated, states that two died from heart disease. Peau met with four severe cases in twenty-four.

There is at first compensatory hypertrophy, later secondary dilatation and degeneration of the heart muscle usually associated with valvular disease. Sibilleau, in seventeen cases of this character, notes that the lesions are usually mitral. The dangers to be apprehended are not only at the time of operation, but later from embolus. We have met with five of these cases, all of them associated with large myomata, and in which no history of cardiac disease preceded the development of the tumor. In two the lesions previous to operation were exceptionally severe, and it seemed questionable whether an operation was justifiable. The convalescence of our patients after hysterectomy was uninterrupted, and three of the cases I was able to examine as to the cardiac condition after the lapse of a year or more. The improvement was most marked, the size of the heart greatly diminished, and the valvular lesions could only be detected by the most careful examination.

Without going into the mooted question as to the nature of exophthalmic goitre, it may be stated that at least some cases result in myocarditis or fatty degeneration of the heart, and perhaps this has been one of the causes of sudden death which follow thyroidectomy. In seven thyroidectomies for Graves' disease we had one death from this cause. The history of the case is briefly as follows :

CASE III. *Thyroidectomy for exophthalmic goitre in patient with myocardial disease; operation performed with local anæsthetic; death in twenty-four hours from cardiac asthenia.*—Miss K. S., aged twenty-seven years, American, occupation, house-work. Admitted to St. Mary's Hospital in May, 1899, with a history of exophthalmic goitre which had appeared a year previously. The severity of the symptoms was gradually increasing. The immediate cause of admission was an ovarian cystoma the size of a fourth month pregnancy. During the period of observation the pulse was constantly above 130, no direct evidence of cardiac lesion. The tumor was removed under chloroform anæsthesia. Recovery uninterrupted, and she was discharged in three

weeks. Readmitted August 29, 1900. The phenomena attending Graves' disease had markedly increased, pulse weak, and constantly above 140, and on exertion 160 or more. There was a faint murmur to be detected at the apex of the heart evidently mitral in origin. The heart was somewhat enlarged and forcible in action. Attacks of dyspnoea were frequent, and the patient very anæmic and emaciated. On September 1st the right lobe and isthmus of the thyroid gland were removed under local anaesthesia with cocaine. The operation was not attended by any untoward accidents. The pulse became exceedingly rapid after the operation and a mild delirium supervened. Twenty-four hours later the patient died from cardiac asthenia.

It will be noted that in the three fatal cases reported one died suddenly forty-eight hours after an easy operation apparently well borne. The second died from the anaesthetic on the operating table and the third twenty-four hours after an operation under local anaesthesia. In going over the records of the cases operated upon in the hospital with which I am connected over 1 per cent. have had some form of heart lesion existing before the operation.

## THE SAFEST ANÆSTHETIC TO USE IN ORGANIC DISEASES OF THE HEART AND VESSELS.

By H. A. HARE, M.D.,

PROFESSOR OF THERAPEUTICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

[Read May 1, 1901.]

It is a remarkable fact that very few people even with grave cardiac and vascular disease die as a direct effect of the anæsthetic. If statistics were looked into it would be found that very few people die from the effect of the anæsthetic in the presence of cardiac disease. A larger number of people die at stool or on going up stairs when suffering from disease of the heart than from the effects of anæsthesia. It will be found that the anæsthetics when skilfully administered usually exercise what might be called a beneficent rather than an evil influence. I am strongly convinced that in the majority of instances when accidents occur during the administration of an anæsthetic the anæsthetic is not to blame for the fatal result, but rather the shock of the operation. My reason for this belief is that I have had some experience in administering anæsthetics to patients suffering from grave cardiac diseases. I have always approached such cases with the feeling that the danger was very great, and I have again and again seen the patient's condition improve under the anæsthetic, so that in fifteen or twenty minutes after the use of the anæsthetic was begun the condition of the patient has been better than before it was employed.

Another point of great interest is the question of the reserve power of the heart in valvular disease, in which there is compensatory hypertrophy. Usually this is not taken into consideration. In healthy cases there is so much energy used by the heart, and there is so much reserve power. In disease we have very little reserve. As a result, as soon as the shock occurs the diseased heart cannot with the small amount of reserve force meet the conditions which are present.

Another point to be considered before taking up the various forms of anæsthetics is the question of poisoning by these drugs. I venture to say that not one surgeon in a hundred has any conception of the quantity of anæsthetic which his patient receives. Careful histories of the operations may show that so many drachms of chloroform or so many ounces of ether were employed, but this gives no information at all to one who really wishes to know how much anæsthetic the patient has received. Some of the anæsthetic goes into the air, and some into the lungs. The possibility of the patient being poisoned because the dosage is unknown or is not estimated is a very important one. Lawrie, in the consideration of this subject, has deserved much credit. He has taken the point that it is not the dose which is poured on to the inhaler, but the dose which is taken into the lungs which should be watched. He has pointed out that in the presence of irregular breathing (in chloroformization this should be the sign for ceasing the anæsthetic until the respirations become regular) there is great danger of an overdose being taken. As soon as the patient takes deep respirations it is impossible for the anæsthetizer to have any gauge of the quantity of the drug absorbed. When a man fills his lungs with a deep breath of ether a large dose is taken, and the next instant on making a superficial inspiration but a small dose is absorbed.

Another interesting point is in choosing particular anæsthetics. Many men do not look into the individual idiosyncrasies and peculiarities of their patients. Dr. Mayo has stated that persons over the usual height are supposed to be the ones who do not take anæsthetics well, and that this is not his experience. I cannot help being impressed with the fact that most of his patients, while probably over height, nevertheless came of exceedingly strong and powerful stock. For a good many years I was near Minnesota, and found that nearly all these large and powerful people are descendants from the Norsemen and the Swedes. The amount of their vitality is extraordinary. They submit to surgical operations and to serious traumatism with apparent impunity. They sustain dreadful injuries in threshing machines, and go through attacks of typhoid fever and other infectious diseases with extraordinary ease. I think the slight ill effects of the anæsthetics in persons over height in Mayo's experience is unusual, and is not of value in influencing our opinion that persons of great height bear these drugs badly. In this part of the country it is correct; in that part of the country it may be incorrect.

Another point which is overlooked by the clinician and surgeon before operation is the examination of the cardiovascular conditions.

In many instances where there is high arterial tension the administration of ether is contraindicated. Ether increases the arterial tension and stimulates greatly the cardiovascular system. So I doubt whether in high tension of the cardiovascular system it is wise to administer ether, though I believe it is as a rule the safest anæsthetic. In regard to the condition of the bloodvessels, I believe American physicians do not employ atropine often enough in the stimulation of the vasomotor system. I have given it frequently in cases and in experiments upon animals. It checks the excessive secretion in the upper air passages and prevents the tendency to œdema of the lungs. Where the respiration is difficult from apparent œdema or diffuse capillary bronchitis it causes a disappearance of the disturbances in breathing which is little less than extraordinary.

The choice of the method by which the anæsthetic is to be administered is more important than the anæsthetic. Several of the surgeons, whom I have considered the greatest, have anæsthetics administered in a way which I think disadvantageous to the patient. They have resorted to a form of apparatus, sometimes connected with an oxygen cylinder, which fits over the nose quite closely. With this is connected a large flat rubber bag. Into this bag the patient expires and inflates it, then inspires and deflates it. He inhales with the anæsthetic a large amount of effete air and carbonic acid gas. It is surely much better to have him exhale into the surrounding air. It has been explained to me by one or two operators that in this way the patient gets more of the anæsthetic and less atmospheric air. I think the patient should be given an amount of oxygen over and above the atmospheric air.

The habit of many of having the oxygen carried to the patient through the anæsthetic has a great many disadvantages. It is probable that the oxygen is capable of producing chemical changes in the drug. When chloroform or ether is used it is impossible to increase the oxygen without increasing the quantity of the anæsthetic, and it is impossible to increase the anæsthetic without increasing the oxygen.

If the oxygen is passed from the oxygen cylinder through a water bottle to the patient's nostril the anæsthetic can be given in accurate dose, and also the oxygen.

In regard to the best anæsthetics, I believe that ether is by far the safest if properly administered, except in vascular disease. It is usually contraindicated in grave vascular disease, in atheromatous conditions, in high arterial tension due to vascular changes. I do not think



ether is strongly contraindicated in Bright's disease if it is impressed upon the anesthetizer that the kidneys are affected and that the ether is to be given with the necessary precautions.

I am much interested to learn from Dr. Finney that Dr. Kelly, who at one time was most enthusiastic in the use of chloroform, has given up its use, because Dr. Kelly told me that he expected to employ chloroform always; that he had found it extremely satisfactory in that it saved time, and he had never had a serious accident.

The use of chloroform in the presence of myocardial change is very dangerous. As Dr. Jacobi has pointed out, it is wrong to suppose that myocardial change is a universal degeneration. Small degenerated patches may be present, and so be overlooked, with fatal results.

Nitrous oxide I believe is very strongly contraindicated in vascular degeneration. I have seen two cases of fatal apoplexy after the administration of the nitrous oxide, principally due to the resulting asphyxia.

In regard to the effect of anesthetics in the presence of valvular and myocardial disease, particularly in valvular disease, I have seen such patients improve by the administration of an anæsthetic. I have taught that in the presence of circulatory disturbances the chances of the patient are better with an anæsthetic than without it. This view has been proved to be correct by the few cases in which I have seen an attempt to employ the various forms of local anæsthesia in the place of general anæsthesia in the presence of valvular disease. I have seen more than one such case in which the shock was so great that the patient's condition was made infinitely worse, and in which the condition improved as soon as the local anæsthetic was discarded and general anæsthesia was employed. One case seen through the kindness of Dr. Keen especially illustrated this. First, spinal anæsthesia was used, then local anæsthesia, and, finally, ether and oxygen. The changes in the condition of the patient formed one of the most interesting things seen in medicine. The woman, pale, lead-color, with pulse almost absent at the wrist, apparently in a desperate strait, under the influence of ether and oxygen instantly revived. The skin, which a few minutes before was livid and lead-gray, showed the restoration of the capillary circulation, so that she went through the whole operation in a successful manner. It is true that after the operation she had grave circulatory disturbance with some tendency to œdema of the lungs. This, I think, was due more to the shock of the operation than to the administration of ether.



In conclusion, I might say from my own observation of intraspinal injection as an anæsthetic that it will soon be regarded as a medical curiosity. I believe it has not the wide scope of usefulness with which it was heralded, and that in a short time it will be relegated to the same obscurity as Bourgeon's method for the cure of phthisis by the injection of hydrogen sulphide and carbonic acid gas into the rectum.

## CARDIAC ACCIDENTS AFTER ANÆSTHETIZATION.

By ALFRED STENGEL, M.D.,

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[Read May 1, 1901.]

PERHAPS the least important subject of our discussion to-night is that which for the sake of completeness I have undertaken to consider. Classifying the cardiac diseases as (1) inflammatory affections of the pericardium, myocardium, or endocardium; (2) degenerative diseases of the myocardium; and (3) disturbance of the cardiac innervation, we may simplify the problem by admitting that as far as our present evidence is concerned there is little to warrant the belief that the administration of anæsthetics in the quantities used by surgeons is capable of producing inflammatory disease, excepting, perhaps, of the myocardium.

Chloroform has been believed by pathologists to be capable of causing fatty degenerations of the intima of bloodvessels and of the myocardium, but it must be confessed that the proof of this view is very questionable, and the thousands of chloroformizations without subsequent disease indicate that such a result is at least a very infrequent one.

It must not be forgotten that the anæsthetics, if they have any power to produce inflammatory or degenerative diseases of the heart, have the best possible opportunity for exercising their deleterious influences, because of their absorption through the lungs and their immediate action upon the heart. If they were capable of producing changes in the tissues generally they would be particularly likely to cause such changes in the heart. It would be easy to demonstrate the effects of anæsthetics upon the heart by administering chloroform or ether to animals in the usual way up to the point of deep narcosis and death, and then examining the heart. Every experimentalist must have had opportunity of studying the heart under these conditions, and degenera-

tions and inflammations have not often been found. It is unlikely, therefore, that the anesthetics have any direct effect of this sort. It is not impossible that a long continued use in small quantities of such substances might effect inflammatory changes of a chronic sort in the endocardium or myocardium, but with such chronic intoxications we have no present concern. It is more likely, however, that the temporary use of anesthetics might increase an existing myocardial disease or even initiate such; and the possibility of disturbing the nervous mechanism of an already diseased heart in such a way as to cause untoward symptoms is manifestly still more likely.

The difficulty in determining the actual cause of cardiac disturbances that follow operations is so apparent that it needs no discussion. The question must always remain an open one whether the anæsthetic or the shock of the operation was the cause of the cardiac disturbances that have arisen after such operation. The only plans for the solution of this difficulty are to draw our inferences from anæsthetizations not followed by operation, and from anæsthetizations with such trivial operations that the shock could not be regarded as a factor of consequence. The former class of cases is so restricted in number that no very accurate data can be obtained. The latter is a more numerous class.

For several years I have been interested in the study of the cardiac conditions before and after gynecological operations, as my attention had been early called to some unexpected results, and through the interest of Drs. Penrose, Beyea, and Hirst the privilege of examining a considerable series of cases was given me. For the purposes of the present discussion this series is a more useful one than would be a similar number of cases of operations in general surgery, as many of the operations were comparatively trivial.

I may classify the results obtained under two heads: First, the results in individuals with valvular or myocardial disease; and second, the results in persons not known to be suffering with any form of cardiac malady.

The former group included quite a number of cases in which a compensated valvular trouble was recognized before etherization, and in which the heart was carefully observed for some days after the operation. In such I have not infrequently found temporary disturbances of action or of compensation of the heart. This has rarely amounted to more than slight irregularity and palpitation, and might perhaps be accounted for by the changed conditions of diet, etc., to which the

patient is subjected after gynecological operations. As a rule, these disturbances of action of the heart have come a few days after the operation, and rarely at the time of the most rigid enforcement of dietary abstinence. I assume, therefore, that it is likely that the operation or the anæsthetization was the cause of the disturbance. I have never seen serious loss of compensation.

In cases of pre-existing myocardial disease which had been recognized, ether has been, as a rule, well borne, and I have seen few cases in which the operation had to be cut short or in which restorative measures became urgently necessary. I have had no experience with chloroform, but, as a rule, these patients have seemed to me to show an improved cardiac condition immediately after the etherization and operation, though some days later there has sometimes been a general flagging of vitality and slow falling off in the strength of the pulse, and in two cases that have come under my personal observation marked cardiac disturbances with sudden death when the operative wound and the original surgical condition had practically healed. One cannot, of course, bring any positive proof that so vague and uncertain a thing as failing strength is dependent upon a weakness of any special organ, but I have the belief myself that in cases of weak heart operations or the anæsthetization incident to them sometimes so increase the weakness of the heart that a falling off in general vitality results.

A recent case that came under my observation illustrates the point I am here making.

A gentleman, aged about sixty-five years, with signs of general atheroma with a slight aortic valve disease, met with a serious accident. I saw him some hours later, and found that he was exceedingly weak, though not exactly shocked. His skin was moist and cool, and his pulse weak and irregular. He was etherized, and his injuries were attended with as little delay as possible, and his condition remained about the same during twenty-four hours. Subsequently, he grew weaker by imperceptible steps, and finally died of sheer exhaustion, without the development of any localized symptoms of any sort. The autopsy showed only fibroid myocarditis and slight aortic valve disease. It seems probable that the nervous shock so disturbed the cardiac action that it flagged increasingly and finally ceased.

Similar cases to this one occur after formal operations. In many of them a terminal pneumonia develops, and this is often ascribed entirely to the etherization or to aspiration of secretions from the throat. While this explanation may be justified in a majority of cases, it does not

wholly suffice to account for the conditions met with. A failing circulation renders the base of the lungs more favorable to the development of a hypostatic pneumonia, and the irritation set up by the ether or by aspirated substances acts as the immediate exciting cause.

Another post-operative result to which I wish to call attention is pulmonary embolism. While at first sight this seems in nowise to be connected with cardiac weakness, it is really more or less dependent upon the state of the myocardium. I have seen several examples and discussed the subject in a previous paper. The gynecologists have particularly directed attention to this subject, as the accident in question has occurred after operations for myoma of the uterus more frequently than after any other form of surgical procedure. The embolus which lodges in the lung originates in a thrombus of the pelvic vessels. The sequence of events, therefore, is: thrombus of the pelvic vessels, pulmonary embolism, embolic pneumonia, death. Sometimes this sequence is completed in a surprisingly short time. The rôle played by the heart in this process is that of a predisposing cause, for unless the myocardium is degenerated, as unfortunately it is degenerated in a large proportion of these cases, pelvic thrombosis does not occur after the operation, and embolism is not, therefore, met with.

While the question of degenerations of the cardiac muscle in uterine or other diseases is of no immediate importance in our discussion, I am tempted to refer in this place to some of the published investigations, because they show the importance of proper activity of the heart after operations if certain grave dangers are to be avoided. The fact that such activity is sometimes wanting is due in the first place to the weakened state of the heart, and in the second place to either the operation or the anæsthetization. The cardiac weakness associated with uterine conditions was first described by Schroeder, and later Hofmeyer<sup>1</sup> discussed the same subject; Säger and Fehling<sup>2</sup> added further observations. The degeneration of the heart found by these observers was most frequently brown atrophy, but occasionally fatty change was recorded. Gessner<sup>3</sup> discusses the subject in detail, and reports seven fatal cases after operation for myoma of the uterus, due to embolism of the lung, and in all of which degeneration of the myocardium existed.

<sup>1</sup> Zeit. f. Geb. u. Gyn., Bd. xl. p. 363.

<sup>2</sup> Beitr. zur operative Behandlung der Uterus Myome. Stuttgart, 1881.

<sup>3</sup> Festschrift für C. Ruge, p. 165. Ueber Tödtliche Lungenembolie bei Gynakologischen Erkrankungen.

Among others he quotes observations of Mahler,<sup>1</sup> who reported six instances with degeneration of the heart, thrombosis, and embolism.

Whether the operation or the etherization is the cause of the disturbance of heart action in these cases is, as I said in the beginning, an open question, impossible of solution at the present time. My own feeling regarding the matter is that etherization should be suspected of playing some part in weakening a previously diseased heart; and I would base this upon my experience in two other cases in which no pelvic thrombosis had taken place, in which there was no cerebral or pulmonary embolism, and in which the fatal termination was more or less unexplained, though the heart seemed from the clinical symptoms, as well as from the post-mortem examinations, to be the organ properly under suspicion. The first case was operated upon by Dr. Baldy for a repair of the cervix. I did not see the patient during life, and was not present at the autopsy, but saw the heart soon after the autopsy. The other organs were reported entirely normal, and at first sight the heart appeared equally so, but its substance seemed friable and resembled in its appearance the condition of the myocardium found in protracted fevers. Unfortunately, microscopical examinations were not made. The second case was one in which ventrosuspension was performed by a skilful operator, and the patient remained in good condition for two days, showing no unfavorable symptoms of any sort. On the third day after the operation the pulse suddenly increased in rapidity, the temperature rose, and in twelve hours the patient died. At the autopsy no abnormality was found in any of the organs excepting the heart, which presented a rather congested appearance, and which, on microscopical examination of a number of portions, examined somewhat after the manner of the serial sections of Romberg, showed intense congestion of the interfascicular capillaries and some acute myocarditis. There was no discoverable cause for this condition of things, and it seemed to me at the time, and has seemed to me ever since, that it was probably the result of etherization.

I am well aware that no positive conclusions are to be drawn from a discussion which has necessarily included many statements of opinion rather than of actually ascertained facts. I think, however, that the following statements may be tentatively made.

1. In all cases of cardiac disturbances after operations it is difficult

<sup>1</sup> Thrombose, Lungenembolie und plötzlicher Tod bei Geburtshilfe und gynäkologische Arbeiten a. d. Kgl. Frauenklinik in Dresden. Leipzig, 1895. Bd. ii. p. 72.

to determine whether the result was due to the anæsthetic or to the operation.

2. In many cases of recognized cardiac disease the administration of ether has a temporarily beneficial effect upon the cardiac condition. It is not improbable, however, that in some of these the secondary effect is an unfavorable one, the symptoms occurring after a lapse of some days.

3. It is important to recognize that certain results following operations, such as basal pneumonia, gastroduodenal disturbances, and especially embolism, are in reality the results of a weakened state of the heart, and that they may, therefore, owe their development to the anæsthetization or to the shock of the operation.

4. The untoward effects of anæsthetics are, I believe, due to the disturbance of the nervous mechanism or the essential muscular automaticity rather than to organic changes in the myocardium, endocardium, or pericardium.



## ANÆSTHETICS IN HEART DISEASE.

BY JOHN M. T. FINNEY, M.D.,  
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[Read by invitation May 1, 1901.]

"In every case in which an anæsthetic is to be administered there are three factors which contribute each an element of uncertainty to the result :

"1. The special action of the agent employed.

"2. The peculiarities or idiosyncrasies of the patient as to susceptibility.

"3. The skill with which the agent is administered."

These words of Sir George MacLeod, spoken some years ago in a discussion on anæsthetics before the Medico-Chirurgical Society of Glasgow, apply with peculiar force to the subject which we are about to discuss.

I wish to make acknowledgment here of my indebtedness to Drs. Tinker, Dabney, Brown, and Pancoast, who, with no little labor, have compiled the statistics for me from the records of the Johns Hopkins Hospital, the Union Protestant Infirmary, and also Dr. Kelly's private sanatorium, which he kindly placed at my disposal.

The literature upon the subject of anæsthetics in general, and their effects, physiological and pathological, upon man and the lower animals, is very voluminous. Carefully recorded observations with reference to the particular effects these anæsthetics have been observed to produce in patients suffering from lesions of the heart are correspondingly meagre.

Much speculation has been indulged in by some writers as to what would take place if certain anæsthetics were administered in certain impaired conditions of the heart, and not a few dogmatic statements

are to be found here and there setting forth the dire calamities which are sure to befall, and that speedily, the luckless surgeon who dares to administer, it may be, chloroform to a weak anemic patient with a dilated uncompensated heart, or perhaps ether to a plethoric arterio-sclerotic with aortic insufficiency. And yet every now and then, in cases of emergency of one sort or another, it falls to the lot of every surgeon to be compelled to administer an anæsthetic to a patient suffering from some serious heart lesion: and one never undertakes such an operation without misgivings.

But that patients exhibiting to a marked degree those conditions supposed theoretically to contraindicate the administration of chloroform will, and do, take it frequently without a single symptom from start to finish—that is, of sufficient gravity to excite a moment's apprehension in the mind of the anæsthetizer—is the common boast of the champions of chloroform. Likewise, the advocates of ether will insist that all classes of patients afflicted with any variety of heart lesion will, as a rule, bear ether well. The weak are stimulated by it, and others

“well,” they say, “at any rate, I have never seen it do any harm, and I have given ether to thousands of cases.” While the advocates of cocaine will tell you that in the form of Schleich’s or other weak dilutions it can be used *ad libitum* in patients afflicted with any form of heart disease without the slightest risk. And so it goes.

It is a waste of time to quote the statistics of Gurlt, von Bardeleben, or the report of the “British Anæsthetics Committee,” as to the relative safety of ether and chloroform, to the man who was brought up on chloroform, has never used anything else, and who has been so fortunate as never to have lost a patient therefrom. According to this man, fatalities are always the result of either faulty administration or failure upon the part of the administrator, in case of the appearance of alarming symptoms, to apply proper remedies. “He neglected to suspend the patient, or to induce artificial respiration; to produce traction upon the tongue, or to dilate the sphincter: to give cardiac massage,” or what not. And nothing can convince the ether enthusiast that the long list of possible complications and occasional casualties that may and do now and then happen, both during and after ether, are caused either by the improper administration of the drug or by neglect upon the part of the attendants to properly protect the person of the patient from exposure to cold and chilling draughts while under the influence of the anæsthetic.

I have found very few careful and satisfactory observations recorded,

showing deleterious effects of anesthetics in heart disease. A study of the fatal cases is of very little assistance, because it will be found at once that but a very small proportion of these cases were known beforehand to have had a cardiac lesion, and the absence of organic heart disease has been proven in a large majority of those cases that have come to autopsy.

Ask the surgeon in active practice the question, "How many of your cases with a known heart lesion of greater or less severity have taken an anæsthetic badly or have exhibited alarming symptoms during the course of the anæsthetization?" I feel sure the almost universal answer would be, "Remarkably few." Indeed, the impression made upon my own mind, without reference to statistics, is that heart cases, so-called, bear ether (my experience has been confined almost exclusively to this anæsthetic) very well, and that the comparatively few cases which have exhibited alarming symptoms while under its influence were those with no evident heart lesion. Notwithstanding this wellnigh universal experience, I venture to say, however, that few careful surgeons undertake without misgivings an operation necessitating the use of a general anæsthetic in a patient the subject of organic heart disease.

It is the object of this paper to show, if possible, whether or not this impression existing in the minds of surgeons as to the comparative freedom from accident in patients suffering from heart disease, while under the influence of chloroform or ether, is well grounded; and if so, why? Is it because in cases with a known lesion the anæsthetizer is more careful to watch closely his patient's condition and be on the alert for the appearance of danger signals; in other words, to give that undivided care and attention to the administering of the anæsthetic to which there should never be, in any case, an exception?

It is a well-known fact that the fatalities under chloroform and ether and the bad effects following them occur much more frequently in the hands of the inexperienced or reckless anæsthetist than in those of the expert. And if it is true that heart cases take anesthetics no worse than normal cases, why should this deep-rooted fear exist in the minds of surgeons as to the danger of giving anesthetics to such patients?

Let us first note what are the physiological effects of these anesthetics upon the normal heart. This having been determined upon, are these effects modified by the conditions found present in the different heart lesions?

Anyone who has had wide experience in the administration of anesthetics must have been struck with the fact that the degree of narcosis

and of danger is not indicated by the actual amount of the anæsthetic used, but by the concentration of the vapor inhaled, since one patient may in the course of a long operation inhale a large amount of chloroform without trouble, while another patient may be thrown into a condition of extreme danger by the inhalation of the concentrated vapor of a few drops. Physiologists tell us, and these conclusions have been accepted by most clinicians, that the effect of the two principal general anæsthetics—chloroform and ether—is practically the same up to a certain point. Their effects, in brief, upon the normal individual are as follows: The pulse, often accelerated before the operation, owing to fright and apprehension, may be still further quickened during the first and second stages of narcosis, although at times it shows some slowing, the effect of reflex stimulation. The deeper the anæsthesia the slower and weaker becomes the pulse; in profound anæsthesia it may be very weak. The tension and rate of the pulse are not so much affected by ether as by chloroform. The margin between a percentage of concentration of chloroform vapor necessary to produce anæsthesia and one likely to produce dangerous results upon the respiratory centre and heart is much smaller than in the case of ether. This is the chief reason why ether is the safer anæsthetic, and why careless and unskilful anæsthetization is so dangerous.

The respiration is not much altered during the first stage. In the second, owing to excitement, it may become irregular and voluntarily suspended for a longer or shorter time, and then deep and rapid inspirations are frequently observed. This is the most dangerous period. Owing to the possibility of a large amount of concentrated vapor being suddenly inspired, the heart may be so injured as to be unable to carry on the circulation. This is the usual cause of sudden death in the early stages of the administration. Later the respirations become shallower and slower, and occasionally in long operations extremely weak and irregular. The respirations under chloroform, as a rule, are less deep than under ether, and the circulation is thus afforded less aid from the respiration.

The action of these two drugs on the respiratory centre seems to be partly direct and partly indirect. The slowing or temporary arrest of the respiratory movements, sometimes noticed in the first stage of narcosis, are ascribed to a reflex action set up by the irritation of the terminations of the trigeminus in the nose and throat, and of the pneumogastric in the larynx and bronchi. But this is of minor importance, except on account of the following deep inspirations which may lead to

the inhalation of a dangerous dose of the anæsthetic if it is pushed at this time. In the third stage direct action of the drug on the respiratory centre is manifested in slow and shallow breathing. If the drug is pushed these effects are increased until finally the respiratory centre becomes paralyzed. And now, although artificial respiration be energetically applied, it often fails, because the heart has become so dilated and the blood pressure so low that the vital centres are so poorly nourished that they can no longer perform their functions, and particularly is this so with chloroform. The effect of chloroform upon the circulation is more rapid and more powerful than ether. They both produce at first a slight rise in blood pressure due to reflex action on the vasomotor centre; later, however, a fall in blood pressure is observed with a slowing of the heart's action, and if the anæsthetic be pushed there is a marked fall in blood pressure and the heart stops beating. This result is probably due to either weakness of the heart or paralysis of the vasomotor centre, probably more often the former. Under a moderate degree of chloroform narcosis the heart may become considerably dilated, while under the same grade of ether narcosis it generally remains unimpaired, and rarely becomes dilated until shortly before respiratory paralysis occurs. Fatty degeneration has been noticed in the heart and other organs after chloroform administration, and if marked may lead to heart failure. This degeneration is so slight in ether that it is of no significance.

"Chloroform is from three to four times as depressant as ether to the central nervous system, while its action on the heart is nearly fifty times as great," says Cushny. Ether, since it has to be given in more concentrated vapor, is more irritating to the air passages, and hypersecretion of mucus, vomiting, etc., are consequently more marked.

As to the actual cause of death, physiologists still differ, but the weight of opinion seems to be that, except in rare instances, respiration fails before the heart. As Cushny has well said, "From a practical point of view it is of comparatively very little importance whether there are a few fluttering beats of the heart after the last inspiration or not. The all-important question is whether the heart has been so injured as to be unable to carry on the circulation, and this is decided by the concentration of the vapor that has been inhaled."

From this it would appear that the most important point in the administration of an anæsthetic, particularly chloroform, is to be sure that the degree of concentration of the vapor inhaled should never reach beyond a certain percentage, say 3 or 4 per cent., while with ether it may be safely carried much higher. It is well to watch the character

and rate of the pulse, but of far more importance to watch the respiration for the earliest indications of danger. Bear in mind, then, the action and effects, physiological and pathological, above enumerated, and the uncertainties attending the use of these agents in a normal individual, and then apply them to the various forms of heart lesions met with, and a very ready explanation is at once offered for the deep-rooted prejudice referred to in the beginning of this paper as existing in the minds of surgeons against administering an anæsthetic in certain of the graver forms of heart disease. One can readily understand how in the hands of the skilled anæsthetist a patient suffering from a mild grade of even the severer forms of heart lesion may take the anæsthetic without exhibiting to the slightest degree alarming symptoms. On the other hand, the possibilities for trouble that suggest themselves in the course of the prolonged administration of an anæsthetic in the case of an individual exhibiting signs of a grave heart lesion are truly appalling. No wonder, then, that the careful surgeon shrinks from exposing his patient to such risks until compelled to by the exigencies of the case.

Heart disease does not of itself contraindicate the administration of chloroform or ether, but it would appear that their administration in the presence of certain lesions is attended with greater risks than with others, and that in certain impaired conditions of the heart the one is to be preferred to the other; for instance, in fatty degeneration of the heart, in fact in all pathological myocardial changes, if at all advanced, it is evident that the cardiac and circulatory changes produced by ether might be attended with some risk, but that chloroform, on account of its greater liability to produce fatty degeneration of the heart muscle, would be especially dangerous.

Since the general effect of ether upon the circulation is that of a stimulant, no class of cases seems especially prohibitive, the contraindications to its use being respiratory rather than cardiac. In aortic disease its effect may be apparently beneficial as well as in slight uncompensated mitral affections. I have myself observed recently in a case of aortic insufficiency the murmur all but disappear and the heart's action improve markedly under the stimulation of ether, as I have in one instance at least observed a mitral systolic disappear completely while under ether, to reappear later after the effects of the anæsthetic had worn off.

It is a cause for wonder that sudden death, relatively so common in heart disease, is not of more frequent occurrence in connection with anesthesia by whatever agent produced, associated as it is with so



many elements calculated to profoundly disturb both the mental and physical equilibrium of the patient, and that this is true, considering to what an enormous number of cases, many of whom are weak and diseased, anæsthetics are being continuously administered, and how few deaths result therefrom, the extraordinary safety of these agents can be the better understood. Cases of sudden death from one cause or another during anæsthesia are, however, to be found scattered here and there through the literature.

Paralysis, arrhythmia, tachycardia, and bradycardia have all been noted as occurring during the course of anæsthesia, due, undoubtedly in some instances, to organic and in others to functional disturbances.

In studying the reports of fatal cases one cannot but feel that in a certain proportion of them at least death was due either directly or indirectly to the violation of some one or more of the cardinal principles underlying the proper administration of an anæsthetic, hence we cannot but emphasize here the especial necessity in all cases of heart lesion of observing the rules formulated from the combined experience, clinical and in the laboratory, of many observers during the half-century of anæsthetization.

Brunton has very well said, "A man is not a horse because he happens to be born in a stable, neither is a death necessarily due to an anæsthetic because it happens to occur during anæsthesia." There are certain well-recognized causes of death independent of the shock resulting from the effects of the operation itself, such as hemorrhage, injury to nerve structures, etc. Mikulicz has called attention to the great importance of blood examination in anæmic patients before operation in order to determine the percentage of hæmoglobin. It has been shown by this observer and the reports of other later writers that in all patients having a hæmoglobin percentage of 50 or less the anæsthetic may produce dangerous results, shock and collapse being very pronounced. When the hæmoglobin is under 30 per cent. the administration of an anæsthetic is attended with grave risk. An interesting case in point is reported by Bloodgood. Interesting observations, although somewhat conflicting, have been made by J. C. Da Costa, von Lerber, and others as to the effect of the anæsthetic upon the red blood-corpuscles themselves. Deaths from fright at the very beginning, or even actually before the inhalation of the anæsthetic vapor has been begun, have been reported. Anxiety and fear are cardiac depressants and may produce dangerous or even fatal symptoms from heart failure.

I have not the time, nor is this the place, to enumerate and discuss all of the principles referred to, but I will, by way of emphasis, indicate a few of the more important in connection with diseases of the heart. It, of course, goes without saying that the usual preliminary preparation, such as fasting, cathartics, removal of foreign bodies from the mouth, etc., should have been attended to before the anæsthetic is begun. The frame of mind in which the patient approaches the anæsthetic is of great importance, and the anæsthetizer should make it a part of his duty to reassure the patient and gain his confidence as much as possible before actually applying the anæsthetic. I am sure that anyone of any considerable experience must have noticed the quieting effect of a few reassuring words upon a nervous patient. I shall say nothing as to the particular mode of administering the anæsthetic. Each anæsthetizer has his favorite inhaler, and each, as a rule, can do better work with that particular one to which he has become accustomed. For myself I prefer a simple cone.

Laborde, Rosenberg, and others have advocated strongly the preliminary application of solutions of cocaine to the nasopharynx in order to lessen as much as possible the reflex action of the anæsthetic upon the terminal endings of the trigeminus, and thus lessen the danger of sudden cardiac syncope. The claims of these writers, however, seem hardly to be supported by other more recent observers.

In selecting the particular anæsthetic which one shall use, whether chloroform or ether, the majority of operators will be governed more perhaps by habit and previous training than by any other factor. Still, there are certain conditions which ought to influence the selection of the anæsthetic, for instance, as a rule, in all cases of weak heart, from whatever cause, chloroform is the more dangerous. It is more dangerous, too, in very nervous apprehensive patients, in kidney diseases, etc., while ether in acute lung affections and alcoholics is more dangerous probably than chloroform.

The physical characteristics and temperament of the patient exert no inconsiderable influence upon the way he takes the anæsthetic. The vapor of ether is so irritating to the mucous membranes of some patients, and the secretion of mucus and saliva resulting therefrom so excessive, that there is actual danger of the patient drowning in his own secretions. Short, thick-necked, fat-jawed, florid men, particularly if of alcoholic habits, are notoriously bad subjects for ether.

Among the other dangers to which the patient is subjected one may mention the beginning of the operation, during the stage of incomplete



anæsthesia. This danger is more pronounced in chloroform than in ether, because of the additional inhibiting effect of pain upon the heart's action. Complete anæsthesia is indicated particularly in cases of shock.

The two greatest dangers to be guarded against are impeded respiration and the administration of too concentrated vapor. In overcoming the former the effect of the position of the patient, the pressure from tight clothing, arms, assistants, weight of instruments, dropping back of the tongue, mucus and foreign bodies in the throat, etc., must all be considered. The skill and experience of the anæsthetizer is of far more importance in preventing the latter than any special form of inhaler.

That the personal equation of the anæsthetizer plays an important rôle in the effect of the anæsthetic upon the patient is very well illustrated in a case of my own :

A middle-aged man was anæsthetized six times in the course of two years by six different anæsthetizers. The length of time of the anæsthetic and the operative procedures in all cases did not vary much, and his general condition, mental and physical, remained practically unchanged. At the first anæsthetization it took one hundred and twenty grammes of ether and eighteen minutes to produce surgical anæsthesia. From the beginning to the end of administration was one and a half hours. Total amount of anæsthetic used, three hundred and ten grammes. Pulse range, 98 to 122.

At the second operation it took one hundred and twenty grammes and fifteen minutes to anæsthetize. Total amount of ether, three hundred grammes. Pulse range, 90 to 132.

Third, five hundred grammes to anæsthetize and twenty-five minutes to produce surgical anæsthesia. Total, one thousand grammes in one and a half hours. Pulse ranged between 92 and 100.

Fourth, one hundred grammes to anæsthetize in twelve minutes. Total amount, two hundred and seventy-five grammes in one hour and forty-five minutes. Range of pulse, 85 to 142.

Fifth, one hundred and fifty grammes in fifteen minutes. Total amount, four hundred and fifty grammes in one and a half hours. Pulse range, 90 to 125.

Sixth, two hundred grammes in fifteen minutes to anæsthetize. Total amount, five hundred grammes in one hour and ten minutes. Pulse range, 100 to 160.

When signs of danger appear remedial measures suitable to the indi-

cations are to be instituted at once. These vary of course with the nature of the trouble. If respiratory failure, artificial respiration must be begun, and if the trouble has come on early in narcosis, the chances of a successful issue are greater than in the later stages.

Here as elsewhere prevention is far better than cure. I firmly believe that the majority of so-called accidents occurring both during and after anaesthesia, from either chloroform or ether, are entirely preventable; that when they do occur it is due to the carelessness or ignorance of the anaesthetist in not properly watching the effect of the anaesthetic upon

NAME	WARD	OPERATION
DATE	ANAESTHETIC	
AMT. TO ANAESTHETIZE TOTAL AMOUNT		TIME TO ANAESTHETIZE DURATION OF ADMINISTRATION
<div style="display: flex; justify-content: space-between;"> <div style="width: 10%;">TIME</div> <div style="width: 45%;">1 HOUR</div> <div style="width: 45%;">2 HOURS</div> </div> <div style="display: flex;"> <div style="width: 5%;">Pulse</div> <div style="width: 95%; border: 1px solid black; position: relative;"> <!-- Grid for Pulse --> <div style="position: absolute; top: 0; left: 0; right: 0; bottom: 0; background: repeating-linear-gradient(45deg, transparent, transparent 2px, black 2px, black 4px); background-size: 40px 40px;"></div> <!-- Y-axis labels for Pulse --> <div style="position: absolute; left: 0; top: 0; bottom: 0; padding-left: 5px;"> 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 </div> </div> </div> <div style="display: flex; margin-top: 5px;"> <div style="width: 5%;">Resp</div> <div style="width: 95%; border: 1px solid black; height: 20px;"></div> </div>		
REMARKS—		
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his patient—and hence, not being quick to act upon the suggestions offered by the symptoms—rather than to the effect of the anaesthetic alone.

I have undertaken the study of one hundred and forty-two cases of patients suffering from different forms of heart disease, and operated upon for different troubles, minor and grave. Some of the operations were attended with a considerable degree of hemorrhage or shock, others with very little of either. I have endeavored to compare the behavior of these cardiac cases with others operated upon for similar affections under as nearly as possible the same conditions, in order to obtain some

idea as to the relative effect of the anæsthetic upon the diseased and normal heart. In the Johns Hopkins Hospital for some years past a regular anæsthesia chart has been kept, showing the record of the pulse-rate at five-minute intervals from the beginning of the anæsthetic to the end of the operation. (A specimen chart is shown on opposite page.<sup>1</sup>)

Of the one hundred and forty-two cases, including organic and functional diseases, there were eight cases of myocarditis. To seven of these ether was given; to one, chloroform and ether. Five took ether badly and three took it well. In the case to which chloroform was administered, it had to be discontinued and ether substituted. The bad effects noted from the anæsthetic were rapid, irregular, and weak pulse, cyanosis, and disturbed respiration. One case, an old woman suffering from general septic peritonitis, due to perforation of the bowels from carcinoma, collapsed on the table and died shortly after, but probably shock and sepsis had more to do with the collapse than the anæsthetic.

There were seven cases of aortic insufficiency. Four were operated upon under ether; in three herniotomy was done under cocaine. All bore the anæsthetic well.

There were six cases of mitral stenosis, four of which took ether, two cocaine, and one chloroform. The operations were all major operations, and all bore their anæsthetic well.

There were two cases of aortic stenosis. In each a complete operation for carcinoma of the breast was performed. Both took their ether exceptionally well, and at the end of the operation little change was to be noted in the condition of either.

There were forty-nine cases of mitral insufficiency, to thirty-eight of whom ether was administered, to nine cocaine, to two chloroform. Five took the ether badly, and five did not take it altogether satisfactorily, although no anxiety was felt during the course of the administration. The nine cocaine cases, consisting chiefly of herniotomies, all did well. The operations in this group were of all sorts. The majority were cases of herniotomy, appendectomy, fistula in ano, hemorrhoids, etc.

There were seven cases of simple hypertrophy, chiefly athletes. Five took the ether well. The sixth, who was operated upon twice, took the ether badly both times. He was a strong, robust young man, apparently in excellent health, but became cyanotic, with rapid and irregular pulse, and a marked ether rigor as soon as he came into the second stage of

<sup>1</sup> These anæsthetic charts were introduced by Dr. H. W. Cushing, former Resident surgeon in the Johns Hopkins Hospital.

narcosis. These operations were chiefly for the repair of accidental injuries, or hemorrhoids, and were not severe.

With functional heart murmurs there were forty-six cases, of whom forty-two took ether, two cocaine, and two chloroform. Of these, seven took the anæsthetic badly. In one the trouble was due apparently to an elongated and hypertrophied uvula, the others from no apparent cause.

There were four cases with a basic systolic murmur, the cause of which was not definitely determined. All took ether; one took it badly. This patient was in a very weak and run-down condition.

There were nine cases of arrhythmia, with no other lesion to be made out. All were given ether; all took it well but one in whom the irregularity of the pulse became more accentuated, but not alarmingly so at any time.

Of twelve cases, the whole number of complete excisions of the breast for carcinoma, in whom heart lesions existed, eight cases of mitral insufficiency, two of aortic stenosis, and one each of mitral stenosis and aortic insufficiency, all took ether well. Of twelve control, normal cases of the same operation, selected at random under as nearly as possible the same conditions, all took ether well. Of six herniotomies under infiltration cocaine anæsthesia, but one exhibited any unfavorable symptoms due to the cocaine. Of six control herniotomies, two exhibited symptoms of cocaine-poisoning.

Of thirty-one cases of herniotomy in patients with various forms of heart disease, fifteen of whom were operated upon under ether, twelve under cocaine, one each under chloroform and eucaïne, and two under a combination of chloroform and cocaine, all but two bore the anæsthetic well; one case of mitral insufficiency developed a rapid, thready pulse and some cyanosis, which gradually disappeared after the withdrawal of the anæsthetic. The other was a case of strangulated hernia which collapsed under ether and later developed a pneumonia.

Of nine cases in whom the appendix was resected, where a lesion of the heart existed, all took their ether well save one, whose pulse became weak and irregular, and respiration shallow, with some cyanosis.

It is manifestly impossible from so few cases to draw any very definite conclusions. But it would seem from a study of these one hundred and forty-two cases, that in the myocardial affections only do anæsthetics exert any markedly bad effects. In valvular disease their influence is very slight, but yet appreciable. In functional disturbances insignificant.

In conclusion, I cannot emphasize too strongly my conviction that in every operation the anesthetist plays almost as important and in some cases a more important rôle than the operator, and one of the reforms most urgently needed in the medical practice of our country to-day is a thoroughly competent corps of anesthetists in our hospitals, and in our medical schools a thorough and complete course of instruction in the proper methods of administration and use of these agents, so powerful for good when rightly used, so useful in the relief of suffering humanity, and yet capable of producing such disastrous results.

Subjoined is a partial list of the authors and works consulted in the preparation of this paper.

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## DISCUSSION.

DR. A. J. OCHSNER, of Chicago: I have been much interested in these excellent papers, and, of course, it is impossible to add anything of value. I will simply speak of some practical personal observations with anaesthetics which I have carried on for some time.

Early in my surgical activity I observed that we never had an alarming condition during the administration of an anaesthetic in patients suffering from demonstrable heart symptoms from organic heart lesions. These people seem to be peculiarly free from alarming difficulties during the administration of the anaesthetic. It did not seem as if the stimulation of the anaesthetic could be sufficient to account for this, and it seemed to me that the deficiency in the heart was more than compensated for by the increased care and attention that the anaesthetist gave to these particular cases, because in all of these cases the anaesthetist was warned. He was more careful in his administration of the anaesthetic, and was more quick to stop its use than if there were no fear of trouble from the heart. It seemed to me, consequently, that it would be valuable to place the anaesthetist in this same frame of mind in all cases, and so, six or seven years ago, I started a system in my own operations similar to that which Dr. Finney has mentioned. In each case the patient was examined three times. The heart particularly was examined three times; first by myself, then by my first assistant, and then by the anaesthetist, who was a graduate, a man for that purpose. The patient was examined generally. His urine was examined, so that the condition of the kidneys was determined, and in each case a special history was kept by the anaesthetist. Since this system has been inaugurated the anaesthetist is more observant of the conditions present, and he is more likely to be left to look after his portion of the work independently. It is my custom to let the anaesthetist look after his portion of the work, being privileged, however, to interrupt me at any time without fear of being scolded for it. My own attention to the anaesthetization is confined to an observation of the condition of the blood. I use the Esmarch mask for chloroform and ether.

There are, then, in the application of anaesthetics in my work only very simple rules which are worked out. The anaesthetist looks after his own work. He is not to be bothered by anyone, with the one exception mentioned. He is to work independently, without regard to my convenience. He is to bear the rule in mind constantly that when the patient has shown any symptoms which do not please him, if they are sufficient to make him desirous to stop the anaesthetic entirely, he is at liberty to do so. He is never to continue giving chloroform under any condition after there has been trouble. Except for the trouble from the irritation of the mucus running to the air passages, I believe ether may be repeated safely. That diffi-

culty is so plain that the anæsthetist can at once recognize it. If the patient becomes blue under the administration of ether this condition obtains. The cases in which alarming symptoms occur are the nervous patients in which the respiration and the heart action are affected directly. In cases of anæmia and in patients suffering from poisoning previous to the administration of an anæsthetic, either from nicotine or from alcohol, the heart does not have the amount of residual force which is required. In these cases we should look for trouble. In two cases out of 5400 death occurred during the administration of the anæsthetic. One was a case of diffuse carcinoma of the perineum coming from carcinoma of the ovary, in which the patient should have been subjected to an exploratory laparotomy. The patient was anæmic, and the anæsthetic seemed to paralyze the respiratory centres. The heart continued to beat for a considerable number of minutes after the respirations had ceased. Artificial respiration was continued for a considerable time, but it never became spontaneous. The other case was one of an anæmic patient in whom the anemia was due to hemorrhage from hemorrhoids.

I think it would be unfortunate should surgeons receive the impression that patients suffering from heart disease are especially safe. I believe they are safe because they are considered especially unsafe.

DR. GEORGE ERETY SHOEMAKER: Cases with valvular heart disease generally stand ether well. I dread far more the cases with chronic vascular changes and secondary renal changes of the chronic interstitial type, which may increase heart difficulties. It is in just these conditions that the routine examination of the urine may fail to show albumin and casts, and the surgeon may be thrown off his guard. Careful determination of the urea would show less than 2 per cent., and a measurement of the daily excretion of urine would show, instead of forty-eight ounces, only twenty or twenty-five ounces. Such patients have a little dyspnoea, which is sometimes considered cardiac, when it is really due to the renal condition, and they will bear an anæsthetic badly. They will not die on the table, but as secondary results of operation they will show often dangerous symptoms. Something has been said about the chronic kidney case being comparatively safe under ether. That may be true of the chronic parenchymatous conditions, but it is the case of chronic interstitial nephritis with low urea that we should dread.

DR. J. WILLIAM TAYLOR: I would like to ask Dr. Finney whether, in the case of death from ether, nitrous oxide gas was used at the beginning, as is generally done by Dr. Kelly. Also, do the patients in Baltimore do badly when ether is given in the hot, moist days of midsummer? I think chloroform is a safer anæsthetic in the hot, moist weather we have in Philadelphia when the humidity runs up to eighty and ninety degrees, and a larger amount of ether is required, it seems to me, to anæsthetize the patient than under ordinary circumstances. The patient is longer in coming out



from under the ether, which is not so easily eliminated at these times. I believe we can get along with a much smaller relative quantity of the anæsthesia on these days in midsummer by giving chloroform carefully and in small quantities.

DR. H. A. HARE: I would like to relate one case which I forgot to mention, and which illustrates the importance of the condition of the vascular system rather than of the heart. The case was that of a woman being operated upon for some abdominal growth. I was asked to supervise the administration of the anæsthetic, which was chloroform. As sometimes occurs when chloroform is administered, the woman became pulseless at the wrist. The abdominal incision was just completed. Following out some recent experiments I had made, I grasped the abdominal aortic vein, compressed it for an instant, and the pulse came back to the wrist. The woman's respirations became regular and she got along well. In a few moments after the circulation seemed to be restored. I took my hand off the vein, and there was again the dangerous condition. The anæsthetic was pumped out of the lungs, ether afterward given, and the patient ultimately recovered.

I am quite sure the patient would have died on the table under ordinary circumstances, and the death be attributed to cardiac failure. This would not have been so, for the heart began to beat as soon as the lungs were emptied of the anæsthetic.

DR. FINNEY, closing: I am sorry that I cannot answer Dr. Taylor's question. The case was related to me. I am under the impression that nitrous oxide was used, because this is the routine practice in Dr. Kelly's department.

## HYDATID DISEASE OF THE BREAST.

By ROBERT G. LE CONTE, M.D.

Read May 1, 1901.

SCARCELY an organ or any portion of the body seems to be exempt from hydatid disease, but one of the organs least frequently attacked is the breast. Owing to its extreme rarity, and perhaps also to the benign course which the disease runs in an organ so superficially situated, our text books and systems of surgery touch but lightly on hydatid disease of the breast, and the subject, if referred to at all, is usually dismissed in a few lines. It therefore seems proper to place the following case on record, as it is apparently the first one to be observed in America, and at the same time to review the literature of the subject, in order that the prominent symptoms of the disease may be brought out clearly. In none of the reported cases was the diagnosis positively made previous to operation, unless a spontaneous opening of the cyst had taken place.

Edna B, a well-nourished mulatto, aged twenty-seven years, was admitted to the Pennsylvania Hospital on March 13, 1899. She was born in Philadelphia, and has spent the whole of her life in that city or in the neighboring one of Camden. No clear history of the diseases of childhood is obtainable. Menstruation began at the age of fourteen and was normal and regular. At sixteen years she was married, and later was the mother of two children, the first born at eighteen years and the second fifteen months later. At twenty-one she had a miscarriage. Shortly after the birth of the first child she noticed an enlargement, with pain, of the right cervical glands near the angle of the jaw; this enlargement slowly spread down the neck without suppuration. A little more than four years ago the right axillary glands also became prominent, with slight pain. Shortly after the axillary enlargement, say four years ago, she noticed a tumor the size of a chestnut in the right breast about two inches above the nipple; this tumor was hard, painless, not adherent to the skin, and freely movable. It preserved these characteristics for two years, during which time it did not increase perceptibly in size, until one day she struck it with the handle of a shovel while working. Rapid enlargement then began, and it was at times quite painful, particularly after a hard day's work. The tumor continued firm and hard until one month previous to admission.

when it seemed to decrease a little in size and become soft. The right cervical glands suppurated and were incised six weeks before admission. On admission, a round, slightly tender, fluctuating tumor, the size of a small cocoanut, occupied the position of the right breast. The skin was normal in appearance and movable over the tumor, except for about an inch surrounding the nipple, where it was adherent, oedematous, and slightly inflamed. The growth could easily be moved over the pectoral muscle. But little breast tissue could be made out surrounding the growth. A small mass of tender and enlarged glands were felt in the right axilla. In addition there was a suppurating sinus on the right side of the neck, which looked tuberculous.

We have the following facts on which to base a diagnosis: A hard, painless, freely movable tumor in a young multiparous mulatto woman, appearing two years after a miscarriage and five years after a chronic enlargement of the right cervical glands. The tumor remained quiescent until subjected to a trauma, when it undergoes rapid growth, but still retains its hardness. The cervical glands break down and suppurate, followed by a softening of the tumor, adhesion to the skin in the region of the nipple, and fluctuation. Three conditions were considered: (1) Adenoma, which had undergone cystic change; (2) tuberculous abscess, and (3) echinococcus cyst. The latter was immediately dismissed on account of its extreme rarity and also because I knew nothing of its clinical symptoms. As the cervical glands were so evidently the seat of tuberculous abscess, the possibility of the breast being the seat of a cold abscess was worthy of consideration. But this diagnosis was also dismissed on account of the long duration of the tumor (four years), its mode of growth, and the absence of sinus formation. A diagnosis was, therefore, made of adenocoele or cystic adenoma, because adenoma is so common in young women, grows slowly and generally painlessly, causes atrophy of the gland from pressure, and sometimes attains large size, even to ten or twelve pounds in weight.

March 15th the patient was etherized and a curved incision made over the tumor to the outer side of the nipple. The sac immediately presented. In attempting to dissect this from the adhesions about the nipple the sac was ruptured and from twelve to fifteen ounces of pus escaped. Some of this fluid was immediately placed under a microscope and hydatid hooklets were found in large numbers. As scarcely any glandular tissue of the breast remained, the breast was amputated together with the enlarged axillary glands. The wound was readily closed with silkworm-gut sutures without drainage, and healed by primary union. The recovery was uneventful.

The pathological notes are kindly furnished by Dr. Simon Flexner:\*

\* The specimen was two years old when given to Dr. Flexner. The alcohol in which it was preserved had been repeatedly changed.

*Wall of Cyst.* The inner lining shows to the naked eye superficial convolutions which, on section of the cyst, present an appearance of polypoid excrescences. These are in immediate contact with the fibrous tissue in which there are islands of glandular tissue. Microscopically the excrescences described consist of a granulation tissue showing different degrees of density; the outward projections are lighter in texture than the intervening tissue where the cells are more compact. The character of the cells is largely epithelioid, but among these cells there are a certain number of the type of Unna's plasma cells. At the line of junction between the fibrous tissue and the granulations there is an almost unbroken layer of plasma cells. The inner surface shows an extensive hyaline transformation of the cells and the intercellular substance. Nothing that can be recognized as such remains of the cuticular membrane. In the forty or fifty sections examined hooklets were not discovered. In the adjacent mammary tissue there is an overgrowth of fibrous tissue.

*Axillary Lymph Gland.* Sections of a moderately enlarged lymph gland show (first) moderate hyperplasia of the lymph cords and (second) extensive hyaline degeneration of the cords and nodes. This latter degeneration affects the interstitial tissue, where it gradually obliterates the lymph cells proper. It also occurs in the walls of the medium-sized bloodvessels. It presents many of the appearances of amyloid degeneration, but it corresponds accurately with Recklinghausen's hyaline degeneration of lymphatic glands. There are no tubercles in the sections.

It is very difficult to get an estimate from the literature of the frequency of hydatid cyst compared with other tumors of the breast, or the frequency with which the breast is attacked in hydatid disease. The eminent writers of the eighteenth and the first third of the nineteenth century classified most of the cystic diseases of the breast under the term of hydatid. Thus, Sir Astley Cooper, in his *Illustrations of Diseases of the Breast* (London, 1829), divides hydatid disease into four separate varieties, and in but one of these divisions does he speak of a parasitic origin. The report of such cases as true hydatids must, therefore, be looked upon with suspicion, unless some positive finding, as daughter cysts, scolices, or hooklets are recorded with the case. After a fairly careful search of the literature I have collected thirty-three cases in which the diagnosis of hydatid disease seems assured. In addition I append some cases where the echinococcus may have been present, but the history does not permit of an exact diagnosis. Of these thirty-three cases the histories are sufficiently clear in twenty-seven to draw some definite conclusions. I have arranged them in the form of a table under headings which seem characteristic of the disease.

Recorder and reference number.	Tumor.					Axil- lary en- large- ment.	Opera- tion.	Remarks			
	Married or single.	Previ- ous births.	First noticed	Position.	Charac- teristics of growth.						
1. Bausi <sup>1</sup>	Single	None.	21 yrs.	Left breast, lower inner quadrant.	Slow.	Egg.	For last few months	Clear fluid, one cyst.	None.	Incision and drainage.	Recovery 21 days, diag- nosed as fibroaden- oma.
2. Bérard <sup>2</sup>	Married	.....	.....	Right breast, lower half.	Slow.	Twice as large as left breast.	Always present	Clear fluid, one cyst.	None.	Sponta- neous opening.	Recovery 25 days, ap- peared 8 months after a blow on breast.
3. Bermond <sup>3</sup>	Married	Preced- ing tumor.	26 yrs.	Right breast.	Slow.	Apple.	None.	Clear fluid, one cyst.	None	Punctur- ed; later incision and seton	Recovery 2 months; had 6 lumps, tumor appeared after fourth; also, had abscess of the breast.
4. Birkett <sup>4</sup>	Married	3 yrs.	23 yrs.	Right breast, inner half.	Slow.	Not stated.	Last 2 months	Pus, one cyst.	.....	Sponta- neous opening.	.....
5. Birkett <sup>4</sup>	Married	Not stated.	40 yrs.	Right breast.	Not stated.	3 in. in circum- ference.	Last 3 years.	Clear fluid, one cyst.	.....	Amputa- tion of breast.	Microscope showed technocoev.
6. Birkett <sup>4</sup>	Married	While suck- ling child.	23 yrs.	Right breast, upper outer quadrant.	Not stated.	4 in. in diameter.	Almost none.	Clear fluid, mother and daughter cysts.	.....	Excision.	Microscope showed booklets.
7. Bryant <sup>5</sup>	Married	3 yrs.	25 yrs.	Left breast, upper half.	Slow.	Cocconut.	None.	Clear fluid, mother and daughter cysts.	None	Incision and drainage.	Recovery 3 weeks.
8. Astley Cooper <sup>6</sup>	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	Specimen in St. Thomas' Hospital, discharged by ulceration from an abscess of the breast, diagnosed as scirrhus.
9. De Haen <sup>8</sup>	.....	.....	.....	.....	.....	Fist.	.....	Cloudy fluid, four cysts.	.....	Excision.	Tumor oblong, irregu- lar, nodular.
10. Dubourg <sup>9</sup>	Married	3 yrs.	22 yrs.	Right breast, lower inner quadrant.	Slow.	Mam- mari- nary.	None	Clear fluid, mother and daughter cysts.	None	Excision.	.....
11. Dubreuil <sup>10</sup>	.....	.....	42 yrs.	Right breast, upper half.	Slow.	Fist.	Last 2 months	Pus, small hydatid cysts.	None.	Incision and drainage.	.....

12. Dupuytren <sup>11</sup>	Married	While suckling child.	28 yrs.	20 mos.	Left breast.	.....	Turkey egg.	Slight.	Clear fluid, daughter cysts.	.....	Incision and packing.	Position of growth vaguely described; may have been in pectoral muscle.
13. Finsen <sup>12</sup>	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
14. Fischer <sup>13</sup>	Single	.....	17 yrs.	4 yrs.	Right breast, upper outer quadrant.	Stationary 3 yrs.	Apple.	Last year.	Mother and daughter cysts.	None.	Excision.	Diagnosed as adenoma; digestive disturbances previous to appearance of tumor.
15. Franceschi <sup>14</sup>	Married	Three confinements. Following miscarriage.	23 yrs.	2 yrs.	Left breast, central.	Slow.	2 by 4 inches.	Occasional.	Clear fluid, booklets.	None.	Excision.	Tumor irregular and lobulated.
16. Franceschi <sup>14</sup>	Married	.....	21 yrs.	18 mos.	Right breast, upper outer quadrant.	Slow.	Turkey egg.	None.	Clear fluid.	Slight.	Excision.	Tumor hard and nodular; pathological examination showed characteristics of hydatid cyst.
17. Graham <sup>15</sup>	Married	Preceding tumor.	.....	7 yrs.	Right breast, upper outer quadrant.	Grew only during lactations.	Not stated.	Last few days.	Clear fluid, booklets.	Present.	Incision.	Tumor appeared after fifth labor; four labors since; grew only during last three lactations.
18. Henry <sup>17</sup>	Married	.....	23 yrs.	5 yrs.	Left breast, lower inner quadrant.	Stationary 3 yrs.	Orange.	Last 2 years.	Cloudy fluid, mother and daughter cysts.	Present.	Excision.	Recovery 27 days; suffered from tapeworm in childhood.
19. Hoppener <sup>18</sup>	Married	.....	35 yrs.	6 yrs.	Left breast, upper outer quadrant.	Stationary 5 yrs.	Fist.	Last 6 months.	Pus, mother and daughter cysts.	None.	Spontaneous opening; later incision.	Intestinal cutarrh for 3 years previous to appearance of tumor.
20. Jonsson <sup>1</sup>	Single	.....	.....	.....	Left breast.	.....	Egg.	.....	One cyst with scrofulous booklets, fluid and daughter cysts.	.....	Excision.	Tumor of several years' duration; patient aged 34 years.
21. Lanenstein <sup>19</sup>	Married	.....	57 yrs.	11 yrs.	Right breast, upper half.	Stationary 8 yrs.	Not to be removed with hand.	None.	Pus, booklets, fluid and daughter cysts.	.....	Incision.	Recovery 9 weeks; married 28 years; mother of 9 children.
22. Le Conte	Married	Miscarriage 2 yrs.	23 yrs.	4 yrs.	Right breast, 2 inches above nipple.	Stationary 2 yrs.	.....	Occasional during last 2 years.	Pus containing booklets.	Present.	Amputation with removal of axillary glands.	Rapid growth followed a traumatism.





Such cases as reported by Warren (*Surgical Observations on Tumors*, London, 1839, p. 205), Roux (*Notizen aus dem Gebiete der Natur- und Heilkunde*, 1828, Bd. xx., p. 351), Fréteau (*Jour. Générale de Méd.*, Paris, 1828, p. 145), Sir Astley Cooper (*Illustrations of Diseases of the Breast*, London, 1829, Part I., pp. 49 and 50) are not placed in the table, because there is nothing in the history which shows them positively to be hydatids, although they have been so considered by other writers. The following cases were also omitted because the glandular tissue of the breast was not involved, the hydatid having its origin in the pectoral or serrate muscle, or within the cavity of the chest, although the tumor presented in the mammary region: Marmaduke Sheild (*Diseases of the Breast*, London, 1898, p. 254), two cases, Gräfe und Walther (*Jour. der Chir. und Augen-Heilkunde*, 1827, Bd. x., Heft 3, p. 375), von Lesser (*Deutsche med. Woch.*, January 7, 1881, p. 7), Landau (*Arch. de Gynecologie*, 1875, t. viii., p. 359), Schnepf (*Rev. Centralb. f. Chir.*, May 13, 1876, p. 304), Gerdy (*Bull. de l'Acad. de Méd.*, 1844, t. x., p. 517), Gardner (*Lancet*, June 8, 1878, p. 851), etc. Many of these cases have been quoted as instances of hydatid disease of the breast. Guermont's (*Rev. Méd. Franc. et Etrang.*, Paris, 1884, p. 73) case, while quoted as a hydatid, was in reality a form of cysticercus. Dupuytren's case has been placed in the table, although the record does not clearly state the situation of the growth, whether in the breast or the pectoral muscle.

STATISTICS. In the United States and Canada, Osler, up to 1891, collected 85 cases of hydatid disease, and Alfred Mann has since added 24 more, making a total of 109 cases. In none of these was the hydatid disease in the breast. In Europe, Davaine, up to 1877, gives a critical analysis of 253 cases, and does not mention one of the breast. Madelung collected in Mecklenburg 196 cases, of which 91 were women, with none in the breast. Cobbald's 136 cases show one in the breast. Böckmann during ten years at the Berlin Charité collected 33 cases, 14 of which were women, with none in the breast. Finsen in Iceland, up to 1869, saw 253 cases, 181 of these being women, with one in the breast. In some combined statistics of Europe, including cases collected by Neisser, Davaine, Finsen, Cobbald, etc., over 1800 cases were represented, and probably 12

or 15 would be a fair representation of the number in which the breast was involved. In Australia, Thomas, up to 1884, collected 1417 single and multiple hydatid cysts, three of which were in the breast, but in 541 the situation of the cyst is not mentioned. Thomas has also tabulated 1897 cases, drawn from European, Australian, American, and Indian sources: 20 of these cases were in the mamma, a percentage of 1.054. Such a percentage seems to me entirely too high, for in combined statistics many doubtful cases creep in which it is impossible for the collector to verify. Without any figures to substantiate it, I believe that 1 per cent. will fairly represent mammary involvement in women between the age of puberty and the period of the climacteric who are suffering from hydatid disease. When we compare hydatid cyst with other tumors of the breast the fraction becomes so small as to be insignificant.

SEX. The condition is confined to women, as there is no record of a case in a male breast.

AGE. The age of the woman at the time the tumor was first noticed varies from seventeen years to forty-two years, with one exception. In this case, reported by White, the woman was fifty-six years of age when she first noticed the growth, but White does not mention whether menstruation was still present or not. No cases in childhood are recorded. We may, therefore, say that the disease begins only after puberty and probably before the climacteric; in other words, during the child-bearing period.

SINGLE AND MARRIED. Of the four single women in the table, the ages of three are noted, respectively, seventeen, nineteen, and twenty-one, the age of highest development of the breast in the single woman. Of the 18 married women previous pregnancies are spoken of in 11, and in 7 no mention is made of the subject. In these 11 cases the tumor was noticed four times immediately after confinement or a miscarriage, the period when the breast is at its highest physiological development. In the other 7 cases pregnancy is noted in 2 two years previously, in 3 three years previously, and in 1 four years previously. In 1 the woman had three pregnancies, but the date of the confinements are not stated. We may, therefore, conclude that the parasite finds a lodgement in the mamma only when that organ is richly supplied with blood.

**BREAST AND POSITION OF TUMOR.** In 18 cases the right breast was involved, in 10 the left, and in 5 it is not mentioned. The position the growth first occupied is mentioned in 22 cases—8 upper outer quadrant, 1 upper inner quadrant, 4 lower inner quadrant, 4 upper half, 2 lower half, 1 outer half, 1 inner half, and in 1 the position is noted as central under the nipple. There is nothing particularly significant about the breast involved or the portion of the organ where the parasite develops, although the upper half seems to be involved twice as frequently as the lower, and the right breast almost twice as often as the left.

**CHARACTERISTICS OF THE TUMOR.** In all cases the tumor was first noticed as a small, hard, movable lump, not adherent to the skin or to the pectoral muscle. Pain was conspicuous by its absence, and even tenderness was seldom spoken of. In many cases the hardness of the tumor was especially referred to. The mode of growth is rather characteristic. In 13 cases the tumor, more or less continuously, slowly increased in size; in the other 10 cases periods of time were noticed in which no perceptible growth occurred. These periods varied from several months to eight and even fourteen years. In two or three cases traumatism was attributed as the cause of the tumor, and in several the previously noted tumor took on a rapid growth after traumatism. In one case two lactations followed the appearance of the cyst; during the first the tumor remained quiescent, but the second seemed to induce a rapid growth. In but one case—White's—were the cysts multiple, one in the right breast and one in the left arm below the insertion of the deltoid muscle. The tumor was usually noted as round or oval, with a smooth surface, but in four it is spoken of as nodular or lobulated, and of irregular outline. Pain was seldom spoken of except in the later stages, and was associated principally with the period of rapid growth. It was these two symptoms—pain and the rapid increase in size—which caused most of the patients to consult a physician. Adherence to the skin or underlying pectoral fascia occurred only in the later stages of the tumor and seemed to be a precursor of ulceration with a spontaneous opening. In one case, beside adherence to the skin, there was retraction of the nipple. Enlargement of the axillary glands was noted in 6 cases; in 1, however, the enlargement antedated the

tumor: in 12 it was noted as absent, and in the remainder it is not mentioned. In no case was fluctuation detected in the growth until it had reached a large size, and even then in some cases the cyst wall was so thick and tense as to give the impression of a solid growth. Crepitation, or hydatid thrill, which is sometimes elicited in echinococcus cyst of other organs, was never noted. Erythema, or urticaria of the skin, the so-called hydatid rash, which has appeared several times after aspiration of a cyst of the liver, has never been seen after aspiration or puncture of a hydatid of the breast. As the cyst increased in size the glandular tissue of the breast atrophied, probably from pressure, so that when the tumor was very large but little breast tissue could be recognized around it.

DEGENERATION AND DEATH OF THE HYDATID. As in other situations of the body, hydatid cyst of the breast is prone to undergo degeneration. When the cyst is large, say from the size of an egg to its largest extent, suppuration is apt to occur in the cyst. The apparent causes for this change may be a traumatism, or applications of stimulating or irritating ointments. When suppuration occurs adhesion of the cyst wall to the skin rapidly follows, with later ulceration and the formation of one or more sinuses. In this way daughter cysts have been observed escaping from what was termed an abscess of the breast. In five of the cases recorded a spontaneous opening of this character occurred, with a discharge of pus and hydatid débris. Under such circumstances the disease will tend to cure itself without surgical interference, although the convalescence may be a very slow one. There is also another mode of death to which the hydatid is liable without the rupture of the cyst wall. As Thomas has pointed out, cases are not rarely encountered in the post-mortem room where hydatid cysts have a solid contents resembling putty in appearance, instead of the usual watery fluid. The microscope shows this putty-like material to consist of fat and granular débris, carbonate and phosphate of lime, cholesterine, hooklets, and broken-down hydatid membrane and scolices. The causes which lead to such a death of the parasite are probably numerous. First. The animal may have reached its natural term of existence, in which case decay and death would follow as a sequence. Second. The production of daughter cysts may be so numerous as to destroy

the mother cyst by pressure. Cases are on record in which collapsed daughter cysts were so closely packed as to resemble the dried raisins of commerce. Third. The growth of the hydatid may be much more rapid than the outer or surrounding fibrous sac. This relative disproportion of growth causes the endocyst to become doubled and involuted on itself, and the fluid which the parasite should contain is replaced by the membrane of the animal; a time will soon come, then, when the food-supply is no longer sufficient to support the life of the animal. Fourth. The outer fibrous sac, like all similar connective tissue growths, tends with advancing age to contract and become more dense, diminishing the calibre of its vessels and interfering with the circulation in its substance, thereby producing degenerative changes which later lead to the formation of calcareous plates. As a result of this degeneration the supply of nourishment to the endocyst is gradually reduced until the animal dies. Of all these probable causes of the death of the parasite the most important perhaps is the condition of the fibrous sac. In one case reported by MacGillivray a cyst the size of an egg was found filled with this putty-like material. In the breast, then, we have examples of both forms of spontaneous cure of the disease recorded. Whenever the contents of a hydatid has altered from a clear fluid, degenerative changes are said to have begun, no matter how slight the opalescence or cloudiness may be. The variations from a slightly turbid fluid to pus or putty material is one only of degree, and they are related as a beginning decay is to a complete one. Of the 24 cases in which the fluid contents of the cyst was noted 16 are reported as clear and 8 as showing some degenerative change in the organism. It may, therefore, be stated that hydatid cysts of the breast are prone to degenerative changes.

It will be remembered that in four of the cases the tumor was spoken of as nodular or lobulated and of irregular outline. In an organ so superficially situated as the mamma it might be expected that the cyst would invariably present a uniformly smooth and rounded appearance, especially as the underlying muscle and chest wall would be the only point of resistance. May not this nodular appearance be explained by the degenerative processes which take place in the fibrous capsule? These degenerative thickenings and

calcareous changes in the sac are never uniform, but vary greatly in different portions of the capsule. If, as they are proceeding, the animal within is also undergoing vigorous growth, the thinner portions of the capsule would stretch and bulge, producing an irregular or nodular contour. The lobulated appearance would simply mean, then, that degenerative changes had begun in the fibrous capsule, and if these changes persisted the nutrition of the parasites would be interfered with and ultimately lead to the death of the organism. We may, therefore, consider the nodular shape as the beginning of a spontaneous cure of the disease.

**SUMMARY.** Hydatid disease of the breast occurs only in women from the age of puberty to the climacteric. It is characterized by the appearance of a small, hard, painless tumor situated in any portion of the glandular tissue of the breast, freely movable with the surrounding breast tissue, either growing slowly or with a more or less long period of inaction. The firmness of the tumor continues until it attains considerable size, and even then the characteristics of a cyst are seldom present. For the most part the growth is smooth and of round or oval shape. Enlargement of the axillary glands, severe pain, irregular outline, and adhesion to the skin are characteristic of inflammation outside of the sac, or degenerative changes in the sac wall, leading ultimately to the death of the organism and a spontaneous cure, either through ulceration or encapsulation. Pain is also associated with rapid growth.

**DIAGNOSIS.** Owing to the great rarity of the condition, the diagnosis previous to operation or spontaneous opening will always be an extremely difficult one. In the young it will naturally be mistaken for adenoma; in the old, when adherence to the skin and axillary enlargement have taken place, a malignant growth will seem probable. It will scarcely be profitable to discuss the various diseases which it may simulate. The diagnosis can alone be positively made with the exploring needle and the microscope.

**TREATMENT.** Although the growth has a tendency to limit itself with a spontaneous cure of the disease, it would never be wise to wait for such a condition to occur, or to attempt to bring it about by the application of irritant or escharotic drugs. Such applications were frequently made a century ago when the dread of the knife



and its consequences were feared. Nor should aspiration be used except as a means of making a diagnosis. The treatment should always be operative, and may be divided under four headings, according to the conditions present:

1. When the cyst is young and not very adherent to the surrounding breast tissue, dissect it out and close the wound without drainage.

2. When the cyst is older and larger, and so intimately connected to the breast that excision would involve a considerable mutilation of the glandular tissue of the mamma, incise the growth freely and evacuate its contents, and then pack or drain, so that granulation may take place from the bottom.

3. When the cyst is quite large, thick-walled, and firmly adherent, but is still surrounded by a considerable portion of the breast tissue, make a partial amputation of the breast.

4. When the cyst is so large that most of the breast tissue has disappeared through atrophy, or when the nipple is involved and adherent to the growth, a complete amputation of the breast should be done.

No death has been recorded in hydatid disease of the breast, not even when suppuration has persisted for months after a spontaneous opening. In other portions of the body hydatid cysts have proved fatal from prolonged suppuration, either from exhaustion or from amyloid changes.

**MODE OF ENTRANCE OF THE PARASITE.** It has been suggested, notably by Dennis, that the parasite may gain access to the gland in the same manner that the streptococci and staphylococci do in abscess of the breast—*i. e.*, through the nipple.\* Dr. Dougan Bird has accounted for the remarkable frequency of lung hydatids in Australia on the ground that the ovum is inhaled and starts its growth directly in some part of the air passages. According to our present views neither of these hypotheses can be correct, for it seems necessary that the eggs must enter the stomach, in order that their envelope may be digested by the gastric juice and the enclosed embryo set free. I cannot do better than quote from Thomas the

\* It has never been proved that bacteria can enter the breast through the nipple, for in abscess of the breast an abrasion of the skin will be found if looked for.



causes that influence the seat of hydatids in the body: "It may naturally be supposed that the liver becomes the most frequent seat of these cysts, because the embryos, after finding their way into the portal vein, here meet with the first obstruction to their passage through the capillary system; but many do find passage through it, and travelling through the inferior vena cava, enter successively the right auricle and ventricle of the heart, and thence by the pulmonary artery reach the pulmonary capillaries, where again a considerable number abide; others run the gauntlet of this second obstruction, and pass by the pulmonary veins into the left side of the heart, and subsequently become conveyed by the current of the systemic circulation to the most remote and varied parts of the body of their host." Such a theory will coincide perfectly with a majority of the cases of hydatid of the breast. If the woman is unmarried we observe the embryo find lodgement in the mamma only when the blood-supply to the gland is at its maximum—namely, shortly after puberty. If it be a married woman, the time of lactation or shortly after it seems to be the chosen moment, when the gland is physiologically in its highest state of development and requiring its maximum of blood. But, as Thomas remarks, it is probable that so simple and mechanical an explanation does not convey the whole truth, for every cystic tapeworm has certain chosen seats in its host, although the echinococcus seems to enjoy the widest distribution of any of the parasites.

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# REPORT OF TWO CASES OF EPITHELIAL CANCER OF THE CHEEK TREATED BY MEANS OF CHEMICAL CAUSTICS.

EXHIBITION OF PATIENTS AND ALSO OF WAX MODEL SHOWING  
ORIGINAL CONDITION.

BY JAY F. SCHAMBERG, M.D.

[Read June 5, 1901.]

As indicated in the title on the scientific programme for this evening, I have the pleasure of exhibiting to you a wax model of the face of an elderly woman, showing a large epithelial cancer of the cheek, and also the patient herself, who comes here to show the results of treatment. I may remark that the wax model is an exact reproduction of the condition as it originally appeared. Such a presentation of the "before" and "after" appearances will doubtless adequately convey to those present the measure of improvement that has been achieved. I am sure that all of you will agree with me that the epithelioma is completely cured.

At an hour too late to permit a change of title on the programme a second case of epithelioma has come under my care. This patient is now under treatment, and I take the opportunity of exhibiting him at this stage.

The history of the first patient is briefly as follows:

E. G., aged eighty-three years, has had a growth upon the right cheek, which began about fifteen years ago as a warty-looking excrescence. During the past five years it has gradually undergone superficial ulceration, at the same time spreading upon the periphery. When the patient first came under observation, in December, 1900, she presented upon the right cheek, below and to the inner side of the malar bone, a crateriform

ulcer about  $1\frac{1}{2}$ " x 1" in diameter, with firm indurated borders and a rolled pearly edge traversed by capillary bloodvessels. The ulcer was covered with a brownish crust, the removal of which excited bleeding. Palpation of the growth showed that the induration extended to a considerable depth into the subcutaneous tissues. The skin surrounding the ulcer had a bluish-red or violaceous coloration.

The patient was given a 25 per cent. pyrogallic acid ointment which was applied for a period of one week. At the end of this time there was a superficial slough present, which when removed disclosed the true depth of the epitheliomatous growth. It was then determined to employ a more active caustic, and a 50 per cent. solution of caustic potash was painted over the part every three or four days for a period of about ten days. Then the stick of caustic potash was applied to the deeper tissues, after previous anæsthetization, with a pledget of cotton immersed in a 10 per cent. solution of cocaine. This was applied several times at intervals of a few days, and finally there was employed for thirty six hours an application of 25 per cent. arsenious acid in powdered acacia, with sufficient 20 per cent. solution of cocaine added to give the mass the consistency of a paste. The parts were then allowed to granulate, a simple carbolyzed petrolatum being used to prevent crusting. A progressive diminution in the size of the ulceration took place, until at the end of four weeks it had completely healed. This was accomplished more through contraction of the tissues than as a result of granulation. It will be noted that the only scar visible is a linear cicatricial trail occupying almost the line of the nasolabial fold. The cosmetic result leaves but little to be desired. While the patient experienced some pain during a part of the treatment, it was at all times quite bearable.

I have also the opportunity of exhibiting a man, aged forty-seven years, who has just above the upper lip, partly involving the ala of the nose, an epithelioma of the type of rodent ulcer. This patient was operated upon about eighteen months ago by an eminent surgeon of this city, but the growth has since recurred at the lower end of the cicatrix. Upon examination with a probe the disease was found to extend almost down to the superior maxillary bone. All of the epitheliomatous tissue has been destroyed upon the surface with an arsenious acid paste, and in the subcutaneous tissue by means of the stick of caustic potash. There is now present a deep but healthy granulating ulcer, which is already beginning to heal from the bottom, and which will doubtless continue to do so until complete cicatrization has taken place.

Time will not permit of any extended exposition of the treatment of cancers of the skin by means of caustics. Suffice it to say that most writers on the subject at the present day regard arsenious acid in a 33, 50 or 75 per cent. paste as the most eligible caustic

for general use. Its employment is accompanied by pain, but this may be, in a measure, mitigated by the admixture of cocaine. It is ordinarily applied, according to the strength employed, from twenty-four to thirty-six hours.

Caustic potash is also useful, more particularly in my experience, in working in the depth of an ulceration. Its action is immediate and powerful, and care must be employed in its use, as it destroys more extensively than is at first apparent to the operator. It disintegrates sound and healthy tissue alike, whereas arsenic exerts a selective action upon diseased tissue.

The use of chemical caustics should be accorded a distinct place in the treatment of cutaneous cancers. Judiciously used in appropriate cases they give eminently satisfactory results. It is far from my intention to disparage surgical treatment in many of these cases. In extensive, deep-seated carcinomata the use of the knife should be strongly counselled. Superficial skin cancers may, however, be equally well or better treated by non-operative measures. The cosmetic result is often superior to that obtained by excision, and the permanence of the cure is equally assured.

Furthermore, many timorous people who would shrink from the idea of an operation would readily submit to a non-surgical treatment of this character.

## DISCUSSION.

DR. J. C. WILSON: Did you anesthetize the patient while applying the caustic potash?

DR. SCHAMBERG: No, I used simply a local anæsthetic. I did not think that a patient of this age should be subjected to the dangers of general anæsthesia. I regarded this case as particularly suitable for the application of caustic remedies. The cheek has now been well for about two months, and I do not think that there is any liability of recurrence.

# SARCOMA OF THE LARGE INTESTINE.

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*(From the William Pepper Laboratory of Clinical Medicine.)*

[Read June 5, 1901.]

MOST of the literature on sarcoma of the bowel and all of the statistical papers on the subject have appeared within the last twenty years. It is probable that, as in the case of sarcoma of other regions, notably of the mediastinum, many of the cases of this rare and interesting disease were classified as carcinomata before the era of accurate microscopical diagnosis. A number of papers on the subject have been published within the last two decades, in which the authors have gradually collected from the literature the scattered cases of this affection.

In 1883 A. Debrunner's<sup>1</sup> inaugural thesis was published at Zurich. In 1884 E. Pick<sup>2</sup> published his case. G. Newton Pitt,<sup>3</sup> in 1889, in a report of a case of lymphoid adenoma of the stomach and intestines, published abstracts of eighteen other cases. (These cases would be included by many pathologists under lymphosarcoma, and they are, therefore, referred to in this connection.) In 1890 Ludwig Orth,<sup>4</sup> in an inaugural dissertation, collected eleven cases of intestinal sarcoma, three of which were of the small and four of the large intestine, and four of the rectum.

M. Baltzer's<sup>5</sup> paper, which is so frequently referred to, and which was the most important and thorough study of the subject which had appeared up to that time (or, indeed, up to the present time, if we

except the paper of Libman, recently published), appeared in 1892. He analyzed eleven cases from the literature and three cases occurring under his own observation in Madelung's clinic in Rostock. Smoler's<sup>6</sup> paper was published in 1898. Nothnagel<sup>7</sup> has a fairly comprehensive paper on the subject in his *System*, in the volume on diseases of the intestine and peritoneum, and Libman,<sup>8</sup> in his excellent article, which appeared in October, 1900, brings up to date the subject of sarcoma of the small intestine, collecting all the literature which he could find on that subject. In 1900 Blauel's<sup>9</sup> paper also appeared, entitled "Ueber Sarcome der Ileocecalgegend"—a collection of eight cases, including two of his own.

The operative side of the question of sarcoma of the bowel has been recently dealt with by Van Zwalenberg,<sup>10</sup> who has tabulated fifteen cases of resection of the bowel for sarcoma.

Of the above-mentioned papers Blauel's is the only one which pays especial attention to any portion of the large bowel. To avoid misunderstanding, however, it must be remembered that the subject of sarcoma of the rectum is not included in the above group. The rectum is the region of the bowel which is most frequently the seat of sarcoma. Clinically it can be well separated, as a rule, from what might more properly be regarded as internal sarcoma, and, according to Paneth<sup>11</sup> and Rosenheim,<sup>12</sup> it differs very little in its manifestations from carcinoma of the same region. We have, therefore, excluded it from our consideration.

The opportunity of studying a case of sarcoma of the ascending colon from a clinical and pathological stand-point having offered itself, we have deemed it of sufficient interest, in connection with a report of the case, to collect and analyze as many other cases of primary sarcoma of the cæcum and colon as possible. To this end we have availed ourselves of a number of cases reported in the list of contributions mentioned above, and collected sundry others from the literature at large.

The following is the history of our case:

John C., aged four years, was first seen at the surgical clinic of the Children's Hospital, March 19, 1900. He was referred from the medical clinic, where he had been under treatment for some time. His history was as follows:

Parents both living and in good health. Mother had been very sickly before this child was born. One other child, an older sister, living and well. The patient, a handsome, fair-haired boy, had no sickness of note until about a year ago. He had had an inguinal hernia



for two and a half years. One year before, in 1899, while in England, he had been very ill, the exact nature of the malady being obscure, except that he presented a prominence of the abdomen (which is still present), and the physician told his mother that the liver was enlarged. For several months past he has suffered from dyspeptic symptoms, has been losing flesh, and is constipated at times. An examination of the patient showed him to be a rather anæmic child, of normal stature, and not much emaciated. The physical examination gave negative results, until the abdomen was reached. This was prominent, and palpation at once revealed the presence of a rather hard mass occupying the anterior median aspect, apparently filling up the umbilical and epigastric regions, and, as far as could be determined, not continuous with either liver, spleen, or kidneys, there being a zone of resonance around it which separated it from the areas normally occupied by these organs. The mass gave the impression of being under or near the anterior abdominal wall, with no intestine separating or coming between them. There were no evidences of ascites.

The diagnosis lay apparently between a tuberculous peritonitis and some form of abdominal tumor. Dr. Samuel Ashhurst examined the case with us, and it was determined to put the child on medical treatment, with the possibility of the condition being a tuberculous one, and to keep him under observation for a time before proceeding to an operation. Inunctions of mercurial and belladonna ointments, equal parts, were ordered, with iron and cod-liver oil internally. The patient was not admitted to the hospital.

A few days later, March 26th, the patient developed a well-marked case of measles, which precluded all thoughts of operation for the time. The urine was examined and found to be negative, the only note being of the presence of abundant amorphous urates. Following the attack of measles, the distention of the abdomen became much greater. On April 1st it was noted that, owing to rigidity of the abdominal walls, the examination of the abdomen was unsatisfactory. There was resonance over the entire surface, and the xiphoid cartilage was pushed forward, protruding beneath the skin.

Following this date a febrile temperature developed, varying from 100.5° to 102.5°, and being highest in the evening. The tympanitic distention of the abdomen became so pronounced as to embarrass respiration, the abdominal walls being rigid, the veins dilated, the umbilicus pouting, but with no ascites. No obstruction of the bowels was present. Food seemed to cause discomfort, and there was evidently

abdominal pain or at least discomfort at other times. Enemata of turpentine and the passage of a catheter were resorted to in order to relieve distention, and on April 8th the child passed, after an enema, a piece of fleshy tissue, about four inches long and less than half as wide, which resembled bowel wall, being thick, of fleshy consistence, and dark red in color. Under the microscope it seemed to be composed of fibrin, but, unfortunately, no careful histological examination of it was made.

Following this the temperature remained elevated for about two and one-half weeks, while emaciation became more and more marked, and the difficulty in feeding increased. The distention, which had been so extreme, became gradually reduced, being apparently lessened by the use of inunctions of mercurial and belladonna ointments and the application of a tight binder. The child was very peevish and resisted examination.

By May 5th the temperature had remained normal for some days, but weakness and emaciation were progressive. He had vomited a great deal for two or three days, and complained of pain at the nape of the neck. There was a somewhat troublesome cough, but no definite pulmonic signs. The bowels moved naturally. There was still some distention of the abdomen at the costal margin, but not much below this. The mass could be again distinctly outlined, but now in the right iliac region. The detection of the tumor had been impossible while the distention was so pronounced.

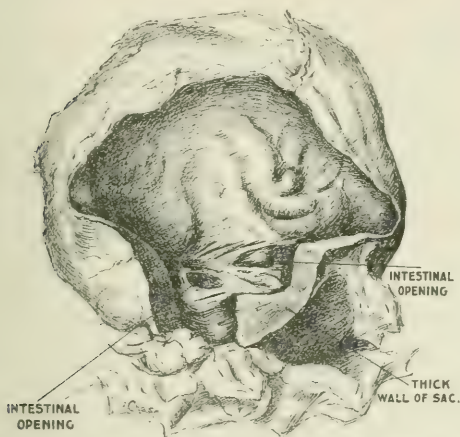
The child now refused almost all food and medicine. A few days later the left foot and leg became swollen and oedematous, and he developed what the mother described as convulsions—spells accompanied with crossing or rolling upward of the eyes, movements of the arms and legs, and followed by coma. Several of these occurred in the twenty-four hours. Examination of the urine showed only a small amount of albumin. Occasional movements of the bowels were noted. On May 14th, after having vomited everything for some days, and with no new symptoms, he died, apparently of asthenia, being emaciated to the last degree. At no time after the unfortunate attack of measles was he in condition to undergo laparotomy, which both the parents and ourselves looked forward to as offering a definite solution of the diagnosis, and perhaps some hope of relief.

*Pathological Notes.* The autopsy was performed twenty-four hours after death, and the following notes made:

The body is emaciated in the extreme. Rigor mortis is only partially developed. The left leg, foot, and thigh are moderately oedematous;

no scars; slight discoloration in the dependent portions of the body. Incision in the median abdominal line reveals a very slight amount of subcutaneous fat. The incision opens up a cavity in the shape of a sac extending from above the umbilicus nearly to the symphysis pubis. Laterally it extends only slightly to the left of the median line, while on the right it reaches nearly to the anterior superior spine of the ilium. The walls of this sac are adherent to the anterior wall of the abdomen, and at this place are about 2 mm. in thickness. To the right and pos-

FIG. 1.



Sarcoma of the large intestine, showing aneurismal sac with the intestinal openings on the posterior wall.

teriorly they increase in thickness; the greatest thickness is about 2 cm., and at the posterior portion of the sac. The walls of the sac are composed of a yellowish-white, homogeneous tissue, of rather firm consistency, the external surface being mainly smooth, except in places here and there, especially posteriorly, where it is somewhat nodular. The inner surface is rather granular. The capacity of the sac is about one pint, and at the autopsy it contained about twelve ounces of a turbid, yellowish fluid, devoid of any special odor.

On examining the inner surface of the sac the posterior wall is seen to present two openings, which correspond with the entrance and exit of the ascending colon. In the space between these two openings, which is about 5 cm. in length, no naked-eye vestiges of the former bowel can be found, the mucous membrane stopping rather abruptly on the surface of the thickened area at the openings of the bowel. Externally the sac is situated about 18 cm. above the ileocecal valve, is pear-shaped, the base completely surrounding the ascending colon, and the apex pointing toward the median line. The only attachment of this sac to the parietal peritoneum is in the median line of the abdominal wall along the line of incision. After removal the sac measured 14 cm. in its vertical by 11 cm. in its transverse diameter.

The remainder of the peritoneal cavity in the immediate vicinity of the sac is free from adhesions. From the tumor, along the mesenteric attachments of the bowel, both above and below the sac, there is much infiltration, the mesentery being in places a full centimetre in thickness. The rest of the abdominal cavity seems quite free from involvement, excepting for a false diaphragm which stretches below the liver, stomach, and spleen, forming a separate cavity for these organs. There is an apparent perisplenitis and perihepatitis which attaches these organs to the diaphragm.

The spleen is not enlarged; the capsule is thickened and in places covered with a distinct yellowish-white exudate. The organ is firmly attached to the diaphragm by dense adhesions. On section the surface is brownish-red in color, and slightly fibroid in character.

The liver is greatly enlarged, of soft consistency, and of a bright yellow color. The outer surface is smooth, with the exception of several small areas which present a yellowish-white exudate, and in a few places it is adherent to the diaphragm. On section it is almost bloodless, and of the same bright yellow color throughout. The gall-bladder is normal.

The organs of the thoracic cavity are to all appearances normal, with the exception of one mediastinal lymph gland, which is distinctly enlarged, and on section is homogeneous, of a yellowish-white color, and of rather firm consistency. There is also a slightly enlarged lymph gland on the thoracic side of the right half of the diaphragm. The lungs show hypostatic congestion, but no evidence of tubercle or new growth.

The kidneys are very much enlarged, the left, which is the larger of the two, measuring 10 cm. in length by 5 cm. in width, and  $4\frac{1}{2}$  cm. in thickness. The capsule strips easily. They both present a slightly

lobulated appearance, with irregular nodular prominences, of a yellowish-white color. The superficial vessels of the cortex stand out quite prominently on this yellowish-white background. On section the surface presents yellowish-white areas, especially prominent in the cortex; these areas are diffuse in places, and in other parts distinctly circumscribed. There are no areas of softening, and the bloodvessels, especially of the medulla, are prominent. There seems to be very little of the normal kidney substance remaining.

The suprarenal glands are not changed in appearance. The stomach appears normal. The small intestine is also normal. The cæcum and the appendix are infiltrated, especially along the mesenteric attachment, with a direct continuation of the growth. The retroperitoneal and mesenteric lymph glands are enlarged; some show the yellowish-white appearance so characteristic of the tumor mass, while others are red and soft.

The sac, with the cæcum and ascending colon, and a part of the ileum, were removed intact, as were also pieces of the liver, spleen, and left kidney, and much of the mesentery, and the enlarged retroperitoneal and mediastinal lymph glands. They were fixed with Müller-formol solution, etc., for further study.

*Microscopical Examination.* Sections were made from the thickest portion of the sac at its base; from its thin upper portion; from the posterior wall, including the afferent and efferent openings of the colon; from the appendix, and the lymphatic glands, peritoneal and mediastinal; from the spleen, the kidney, and the liver. Sections from the thickest portions of the sac are covered on the outer surface with peritoneum, and are composed of a reticular fibrous network, aggregated here and there into denser masses of connective tissue. The meshes of this framework are densely packed with small, round, mononuclear cells, the nuclei of which take the stain moderately well and show very distinctly a chromatin network, some also showing evidences of karyorrhexis, and here and there mitotic figures. Surrounding the nucleus is a very small rim of protoplasm. In the denser portions of the connective-tissue framework are bloodvessels of moderate size, with fairly well-formed walls. The rest of the tumor contains small capillaries with distinct walls. Near the inner surface of the sections of the thick portion of the sac are vestiges of smooth muscle fibre, which are only recognizable as bundles in a few places, owing to separation of the individual fibres by the infiltration of the round cells previously described. This area of muscular tissue remaining is quite close to the internal surface of

the sac, showing that the mucous membrane and submucosa have sloughed away.

The thin portion of the sac in relation with and adherent to the anterior abdominal wall is covered with peritoneum, and shows itself on section to be composed of two layers—the outer is composed of fibrous tissue, with few nuclei among the connective-tissue bundles; the inner, made up of fibrous tissue infiltrated with chains of the special round cells described. The walls of the bloodvessels here are also well formed. The juncture of these two layers is more or less defined, though in places the infiltration to the fibrous layer is quite evident.

A longitudinal section taken from the posterior wall of the sac, between and including a portion of the afferent and efferent parts of the colon, in connection with the sac, is covered with peritoneum. At each end of this section the bowel is about normal in appearance, excepting for a very slight subperitoneal infiltration of the tumor cells. As we approach the centre of this section, a point corresponding with that portion of the sac between the ends of the bowel, the layers of the intestine become more and more separated, and their appearance altered by the increasing infiltration of the new cells. In the mucous membrane the tubules become shorter and further apart, and, finally, rather abruptly disappear. The muscularis mucosa gradually disappears, but the bloodvessels seem to become more numerous and greatly dilated. In places they have an angiomatous arrangement. The muscular layer, as above mentioned, comes near the surface as the other layers disappear. The individual bundles are greatly infiltrated, so that in the middle of the thickened area only an individual fibre is occasionally seen.

In the region where the sac springs from the colon, and where the tumor infiltration completely surrounds the bowel, the new growth pushes its way between the two layers of the mesentery. Along the cæcum this makes a partial mantle, and on reaching the appendix completely surrounds the entire length of this organ. This surrounding mantle is in places thicker than the intestinal wall itself. The appendix is infiltrated in all its coats, to such an extent in some sections that the normal structure is scarcely to be recognized. In one of these sections an area of degeneration resembling caseous material is to be seen. This is the only area of degeneration found in the tumor.

The lymphatic glands of the mesentery in the region of the tumor are enlarged, of moderate size and consistency, and on section they show a homogeneous structure of whitish color. Microscopically the capsule of the gland and the fibrous trabeculae show distinct thicken-



ing; in places the capsule is distinctly infiltrated with the small round cells, and in some glands there is a mantle of round cells surrounding the gland.

The fatty tissue of the mesentery between the glands shows tracts and heaps of small round cells.

The same structure was observed in the isolated enlarged gland of the mediastinum and in the enlarged gland found on the thoracic side of the diaphragm.

FIG. 2.



Section of bowel wall, with subperitoneal growth

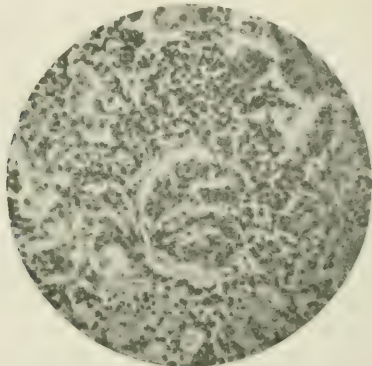
*Spleen.* The capsule and trabeculae are distinctly thickened; the Malpighian bodies appear to be slightly enlarged, but they are not distinctly outlined. What was at autopsy thought to be a perisplenitis is found to be a deposit of small round cells similar to those of the tumor.

*Kidney.* The nodules observed arising from the surface of the kidney are composed of almost pure tumor tissue. They exceptionally



show an altered glomerulus, as the only remains of the former kidney substance. Between these nodules the kidney structure is more in evidence, although the tubules are separated by the infiltrating tumor cells. The cortex is greatly thickened, this thickening being due to the new growth. The medulla is less involved, and the tubules of the pyramids in many places show only slight changes. The tubules, especially in the cortex, show cloudy swelling, fatty degeneration, necrosis, and in places desquamation of the lining epithelium.

FIG. 3.



Section of kidney, showing glomerulus and infiltrating tumor cells.

*Liver.* The sections of the liver present a remarkable degree of fatty infiltration and degeneration; in fact, these changes are so pronounced that a normal liver cell can scarcely be seen. Along the interlobular connective tissue, especially surrounding the vessels and ducts, there is a beginning infiltration of the new growth.

Nearly all of the writers on sarcoma of the intestine have prefaced their remarks with comments upon its rarity. Statistical proofs of this are easily found. According to Baltzer,<sup>5</sup> Stort found no cases of sarcoma of the bowel in the records of the Berlin Pathological Institute from 1859 to 1875. Baltzer analyzed fourteen cases, three of his own and the rest collected from the literature. Nothnagel<sup>7</sup> dwells on the comparative infrequency of intestinal sarcoma compared with carci-

noma. In the Wiener Allgemeinen Krankenhaus, from 1882 to 1893, of 2125 autopsies on cancer cases 243 were of the bowel. Between the same periods, of 243 sarcomata only 3 were of the bowel. He quotes Müller, who found in Berne, of 521 cancers, 41 of the intestine, and of 102 sarcomata but 1 of the intestine, the ileum. Smoler,<sup>10</sup> in fifteen years, from 1883 to 1898, out of 13,036 autopsies found 13 cases of primary sarcoma of the small intestine—a proportion of 1 to 1000. Libman was able to collect about 59 cases in all of sarcoma of the small intestine.

When we compare the relative frequency of sarcoma of the large with that of the small intestine, we find it universally admitted that the latter constitutes the larger class numerically. Disregarding for the present the difference between lymphosarcoma and sarcoma, which, as Nothnagel says, while pathologically distinct, cannot be separated clinically from each other in this locality, we are able to collect the following data: Of 12 cases mentioned by Nothnagel, 1 was duodenal, 3 in the jejunum, 4 in the ileum, 3 in the cæcum, and 1 in the rectum. Nothnagel remarks on the difference between sarcoma and carcinoma of the bowel, the favorite seat of the latter being in the large intestine. This difference is present, he says, at least in the case of lymphosarcoma, to which class 9 of the above tumors belonged. Of Smoler's 13 cases, 2 are included in our list as probably primary in the large intestine, although he includes them in his table of small intestine cases. Treves<sup>13</sup> says that lymphosarcoma is rare in the colon alone, and much more common in the small than in the large intestine. Of 18 cases, in 5 the tumor was located in the stomach, small intestine, and colon; in 1, in the stomach and small intestine; in 3, in the small intestine and colon; in 8, in the small intestine alone, and in only 1 case in the colon alone. He gives the ileocecal region as a common seat, and states that the tumors grow largest in this locality. Excluding the rectum, he gives the small intestine as the most common site of sarcoma, which, he states, is very rare in the colon. The relative frequency is given by Rosenheim<sup>12</sup> as first in the rectum, and next in the small intestine. Of Blauel's<sup>9</sup> 8 cases of sarcoma of the ileocecal region we have included 6 in our table as primary in the cæcum. Of 10 cases of sarcoma of the intestine studied by Ablon,<sup>11</sup> 2 were in the large bowel. Libman states that sarcoma by preference occurs in the small intestine, and that in the large intestine (always excepting the rectum) they are much less common, and he quotes Krueger as follows: Of 38 cases, 16 were in the small intestine, 1 in the ileum and cæcum, 2 in the cæcum, 1 in the

appendix, 1 in the transverse colon, 1 in the small and large intestine, and 16 in the rectum.

Libman collected 59 cases of sarcoma of the small intestine; we have found in our search but 22 cases of sarcoma of the large intestine. We have analyzed these cases as far as the data we could secure permitted, with the following results:

**AGE.** The age of the patients ranged from under two years to over sixty. There were seven under ten years; certainly two and probably three between ten and twenty years; four between twenty and thirty; five between thirty and forty; one between forty and fifty; one between fifty and sixty; and one over sixty. The first decade contained the greatest number; the fourth decade the next greatest. There were only three cases past forty years of age.

**SEX.** The cases were nearly equally divided in point of sex, there being 12 males and 10 females.

**LOCATION.** Of the 22 cases which we have tabulated as primary sarcomata in the large bowel, in 5 the primary location was open to some doubt, there being, however, a strong probability that it was in the large intestine. In 2 of these there was involvement of the last portion of the ileum. In 1 case—that of Lange—no other part of the intestine was involved, but the growth may have been primary in the ovaries, which were sarcomatous. In 3 other cases, while primary in the large bowel, it involved the ileum by extension. In the remaining 14 cases the large bowel alone was the seat of the sarcoma. When we study the location of these tumors more in detail we find that in 7 cases they were confined to the caecum (including with it the ileocecal valve and the appendix); in 5, the caecum and the ileum were affected; in 3, the caecum and ascending colon; in 4, the transverse colon; in 1, the descending colon, and in 2, the sigmoid flexure. The caecum is thus seen to be the most common seat, the next in frequency being the caecum and ileum; the ileocecal region comprises the seat of 12 out of 22 cases, or 54.5 per cent. The transverse colon stands next, being the primary seat in 4, or 18.1 per cent.

**SIZE.** In 8 the size was not stated; in 1 it was said to be the size of a man's head, while in 3 it was the size of a child's head; in 1 it was compared to a cricket-ball. Briefly, the tumors ranged in size from that of a hen's egg to that of a man's head. In one case the growth was in the form of a ring causing partial obstruction.

**VARIETY.** In tabulating the tumors from the morphology of the cell we have preserved separate columns for small round-cell sarcoma and

lymphosarcoma, although it is difficult to make any definite boundary between these two classes. Where the reporters have described them as such, or from their histological examination they have seemed to us to fall in this group, we have included them as lymphosarcoma; where they have been described as small round-cell sarcoma we have classified them under this head. In 2 cases the type of cell was not stated. Of the remaining 20, 10, or 50 per cent., were round-cell sarcomata; 9, or 45 per cent., were lymphosarcomata, while 1 was of the spindle-cell variety.

**METASTASIS.** Of 19 cases in which the data as to metastasis was given the abdominal lymphatic glands were involved in 13, or 68.4 per cent.; the peritoneum in 5, or 26.3 per cent.; the small intestine (by metastasis, not by extension) in 2, or 10.5 per cent.; the lung in 2, or 10.5 per cent.; the kidney in 2, or 10.5 per cent.; the spleen in 2, or 10.5 per cent.; the liver in 3, or 15.7 per cent.; other glands in 2, or 10.5 per cent.; the epididymis and spermatic cord in 1; the mesentery (subperitoneally) in 1; the orbit in 1, and in 1 case there was a secondary growth in the large intestine. In 1 case there was no metastasis, and of the 3 cases in which the data was wanting 1 *case recovered after operation*.

The abdominal lymphatics are thus seen to be by far the most common sites for the deposit of metastatic growths, with the peritoneum next in point of frequency. Except where the peritoneum is involved by continuity the road of dissemination of the infecting cells is through the mesentery, and this would explain the frequent and early involvement of these glands which was present in many of the cases at autopsy and in those subjected to radical operation.

**ETIOLOGY.** The etiology is as obscure as is the case in internal malignant diseases elsewhere. In at least two of our cases there was a strong family predisposition to malignant disease, and there was a history of abdominal traumatism of doubtful influence in two others. Flexner<sup>15</sup> and Libman<sup>8</sup> have called attention to peculiar bodies which they detected in sections from lymphosarcomata of the stomach and small intestine, which they regarded as possibly standing in the relationship of causative organisms.

**ORIGIN OF TUMOR.** The place of origin of the above tumors is rather difficult to locate on account of the size of the tumor and the involvement of the bowel when the subject presents itself either to the operator or to the pathologist; but from the data of the microscopical examination of the tumors which we have been able to collect, and from the careful examination of our own case, it seems to us that the mucosa or submucosa is the starting-point of these tumors, and, from the normal

histology of the intestine, either may be the origin if we take for granted that they have their origin in the lymph follicles. From the mucosa or the submucosa they involve the other coats—the muscular offering the greatest resistance, and, though always infiltrated, traces of this layer are usually found, sometimes as the only remains of the former gut. The subserous coat, from its position, offering very little resistance, we find the greater mass of the tumor usually between the peritoneal covering and the remains of the muscular coat. The serosa itself is rarely perforated. This corresponds with what Baltzer pointed out years ago as the behavior of these tumors in the small intestine. The absence of stenosis and the frequent occurrence of dilatation, sometimes even aneurismal in character, as in our own case, has been explained in the small intestine by the early infiltration and paralysis of the muscular fibres, and the consequent dilatation by accumulation of feces. However, the early involvement of the submucosa, with its plexus of nerves, must not be forgotten as possibly a potent factor in this dilatation.

The *alterations* produced in the segment of bowel involved may be classified as, first, involvement of the whole circumference of the bowel in a rather limited space, forming a rounded tumor with or without dilatation of the lumen. This is the most common condition. The dilatation may be actually aneurismal in extent, due to stretching of the infiltrated wall or to extensive ulceration and breaking down of the interior of the tumor. In about 20 per cent. of these cases the tumor was situated only on one side of the gut. Again, the bowel may be converted into a thick-walled tube, the infiltration extending over a considerable distance in the bowel. In the transverse colon the tumor tends to proliferate in the great omentum, the bowel losing itself in the mass. In only one case was the tumor of the narrow, ring-shaped, stenosing type often seen in carcinoma.

**DEGENERATION.** The common degeneration of the tumor consists of ulceration of the mucous membrane over the tumor mass, softening within the tumor mass, and subsequently cavity formation. This softening may lead to perforation, with direct communication to the peritoneum, and suppurative peritonitis (in one case purulent peritonitis was found without discoverable perforation), or perforation may follow adhesion between the tumor and loops of the small intestine, as in Blauel's second case (No. 18).

**SYMPTOMATOLOGY.** In 5 of the 22 cases little or no clinical history was obtained from the sources at our command. Emaciation was mentioned as being present in 11 cases; in 10 it was not mentioned;

in 1 case it was not present. It is thus seen to be a frequent symptom, as might be expected from the nature of disease. In our case, as in several others, it was extreme. In the case in which it was not present death was due to septic peritonitis, and not to cachexia and exhaustion, which are common causes of death.

FEVER was present in 9 cases, usually a moderate elevation, especially noted before death. In 1 case, in which there was a secondary infection (probably with the bacillus *aërogenes capsulatus* and another organism), there was high fever, running up to 104.4° F. for the last four days of life.

EDEMA of both lower extremities was present in 1 case, and of the left lower extremity in our own. Pressure upon the iliac veins might, with general weakness and position, be considered as the cause. Ascites was very rarely present.

TUMOR was detected in 16 cases. It was not detected in 2, not noted in the history in 3 (although 2 of these were operated upon, and in 1 no data were obtainable (Hofmokl, Case No. 21). The presence of a tumor is thus seen to be a most noticeable symptom.

The *locality* in which the tumor was detected during life varied considerably. In 7 it was outlined in the right iliac fossa, in 1 of these cases there being two other tumors in other localities. In 2 it was primarily in the median umbilical region, one of these later shifting to the right iliac fossa, and the other extending over the greater portion of the abdomen. One was in the epigastric region, and 4 were situated to the left of the median line, 1 being in the left umbilical region, 1 in the left hypogastric region, and 2 in the left hypochondriac and left lumbar regions. The frequent presence of the tumor in the right iliac region corresponds with the frequent ileocecal location of the growth. In all of the 7 cases in which the tumor was observed to be situated here, the ileocecal region was found to be the site of the tumor, with 1 exception, that in which 2 other tumors were detected during life, in which the transverse colon was the primary site, and in which there were numerous metastatic growths. The next most common location was to the left of the median line. Of the 2 cases observed in the left umbilical and hypogastric regions, 1 was of the transverse colon, and 1 of the sigmoid flexure. Of the 2 in the left hypochondriac and lumbar regions, 1 was a caecal tumor with intussusception of the ileum and caecum into the colon, and 1 was of the sigmoid flexure. The epigastric tumor sprang from the ileocecal region of the bowel, and here, also, there was intussusception. Of the



2 in the umbilical region, 1—our own case—was of the caecum and ascending colon, which afterward shifted to the right iliac region, and 1 was a tumor of the transverse colon. The sarcomata of the caecal region of the large intestine are thus seen to be usually observed in the corresponding area of the abdominal surface, but may be detected in the median line, or, where there is an intussusception, in the epigastrium or left hypochondrium and left lumbar region. Tumors of the transverse colon usually occupy a median position, sagging downward; tumors of the sigmoid may be looked for to the left of the median line.

In the majority of cases in which the clinical symptoms were given the tumor was described as hard, sometimes of a smooth and sometimes of a nodular feel, rounded or flat, and in two cases there was a sense of fluctuation elicited on palpating it.

*Mobility.* It was more than twice as often stated to be movable as immovable, and in 2 cases it is noted that it moved with respiration. The liver was sometimes displaced.

The tumor was frequently found to be *tender on palpation*.

**GASTRO-INTESTINAL SYMPTOMS.** These were mentioned in 14 cases, or 63.6 per cent. They were mainly pain, anorexia, and vomiting. Pain was present in the majority of cases; in fact, in only 1 was it stated to be absent. Several other incomplete cases made no reference to it. In 3 it was increased on taking nourishment, and in 1 during urination. It was twice the first symptom noticed, and it was often severe, periodical in some, acute in some, and colicky in others. It was always referred to the abdomen, but not always to the tumor.

In 3 cases it simulated appendicular pain in character and location, and in these cases the tumor was in the ileocecal region.

Other occasional symptoms were: bloody stools, 3 cases; diarrhoea, 2 cases, and general dyspeptic symptoms were present in 9 cases.

**OBSTRUCTION.** The absence of obstruction in the large majority of cases is one of the striking characteristics of this form of malignant disease of the large bowel, and is a characteristic which it shares with sarcoma of the small bowel, and which separates it sharply from carcinoma of the same locality. It was certainly absent in 13, or 59 per cent., and it was not noted in the history, and, therefore, probably absent in 6 cases. It was complete in 1 and incomplete in 1, and in 1 the clinical history was not obtainable. In 1 of the 13 cases obstruction was present once during the course of the disease, from twisting of the tumor, as the symptoms disappeared after manipulation; hence obstruction in its truest sense did not exist in this case.



In the case of complete obstruction (Horn) the seat of the tumor was in the descending colon. It was the only case of the spindle-cell type, and the obstruction was due to almost complete stenosis, with impaction of a small fecal mass. In the case of incomplete obstruction, one of Debrunner's (Case No. 4), the tumor was a ring-shaped, round-cell sarcoma of the sigmoid flexure. Thus the only tumors producing obstruction were located in the descending portion of the large bowel.

Obstruction in this class of tumors involving the small intestine has always been due to intussusception, volvulus, or adhesions. In 2 of our series of cases *intussusception* was found (both tumors of the ileocecal region), and in neither did it cause obstruction.

**DISTENTION.** While not a constant symptom this was observed quite frequently, being especially noted in eight cases, often in a marked degree; in one case only was it due to obstruction.

**APPENDICITIS SIMULATED.** In Libman's paper on sarcoma of the small intestine he reports five cases, in three of which the clinical picture was very similar to that considered diagnostic of appendicitis. He lays much stress on this important clinical observation, and remarks that in attempting to ascertain whether such resemblance had been noticed before he found that the clinical picture was an unknown one. He is not the first, however, to call attention to the fact that sarcoma of the bowel may closely simulate appendicitis. Orth,<sup>4</sup> in 1890, in speaking of the diagnosis of sarcoma of the intestine, dwelt upon the difficulty in separating some cases of typhlitis and perityphlitis from it. Wharton,<sup>16</sup> in 1892, published a paper entitled "Sarcoma of the Cecum Simulating Appendicitis," and in the case he reported exploration was necessary to differentiate between these conditions (Case No. 11). He personally narrated to us the history of another case, in which the resemblance was as striking (Case No. 12). In one of Blauel's cases, also, is an attack of supposed appendicitis noted as preceding the discovery of the tumor. The fact that the appendix is very often the seat of infiltration in ileocecal growths may be partly responsible for the symptoms.

There are practically no data in the cases which we have collected in reference to the condition of the blood, although the patients were often said to be anæmic. One case (Fisher, Case No. 19) gives the blood examination three days before death: Hæmoglobin, 50 per cent.; no poikilocytosis or leucocytosis. There is a similar lack of data in the urinary examinations. In our own case albumin was noted late in the course of the disease. In Baracz's case blood cells and blood casts

were present in small quantity, without involvement of the kidney. In two cases the urine was normal.

**SECONDARY INFECTION.** In Fisher's case (No. 19), where the sarcoma was located in the cecum, the patient, a male, aged twenty-eight years, first detected the tumor three weeks before admission to the hospital. One week later he developed abdominal pain, followed by swelling of the gums and bleeding, and later by the appearance of a purpuric rash liberally scattered over the front of the body and the neck and arms. Epistaxis was present. The blood showed 50 per cent. hemoglobin, and no leucocytes or poikilocytes. There was irregular fever during the three days he was under observation in the hospital. He died, and at the autopsy the subcutaneous tissues, especially of the neck and scrotum, and the peritoneal cavity, were distended with gas; and there were small gaseous cysts scattered thickly through the tumor and the spleen, and present in the liver, and to a less extent in the kidney. Aërobic cultures were sterile; anaërobic not made. Microscopically many bacilli were found in the growth among the sarcoma cells around the cysts, often in pairs, and showing a clear space—probably an unstained capsule—around each bacillus. He regarded this germ as probably the *bacillus aërogenes capsulatus*, and the infection as probably a mixed one. He refers to the case of Hilton Fagge as showing the association of sarcoma with purpura. He thinks the sarcoma acts by lowering resistance and, at the same time, providing a portal of entrance for the germ. Hilton Fagge's<sup>17</sup> case was one of sarcoma of the end of the ileum and the ileocecal valve, and the symptoms bore a striking resemblance in some points to those of Fisher's case just described. It is not included in our list of cases. The symptoms were entirely those of secondary infection. After some exposure the patient suffered for several weeks from scattered pains in some of the joints, especially the hips and shoulders, without effusion, and had fever and acid sweats. When admitted to the hospital about a month later he was supposed to have rheumatic fever. He then developed a purpuric rash, with hæmaturia, great swelling of the eyelids and scrotum, and ecchymosis of the conjunctivæ. Nodules appeared at the sites of some of the purpuric spots. After death, about two months after the onset of the symptoms, decomposition rapidly set in, and sixteen hours later, at the time of an autopsy, was quite advanced. The scrotum, thighs, and upper arms were emphysematous. The nodules in the skin proved to be sarcomatous.

**DURATION.** It is difficult to estimate the duration of the disease in this class of cases, as in all of internal malignant disease where the his-

tory and the symptomatology have to be depended upon, for the new growth is undoubtedly present for some time before the patient or the physician discovers it. Hence the duration can be estimated only from the time of onset of the symptoms. In the cases not subjected to radical operation, the duration of life varied from one to eighteen months; in the cases in which a radical operation was performed, the duration of symptoms varied from one week to five years before operation, although in the latter case the tumor had been observed for only eight months. One case not operated upon gave no definite symptoms until obstruction developed a few days before death.

The usual causes of death in non-operative cases were cachexia and exhaustion. These were noted in at least 6 cases—in 1, associated with recurrence after the operation. In another case with wide-spread metastasis the cause of death was given as heart failure; this was also probably due to exhaustion. Two cases died of purulent peritonitis, probably due to infection from the bowel; in 1 of these cases there was incomplete obstruction. One case died of acute obstruction, and another from mixed infection (purpura hemorrhagica).

Fourteen of the 22 cases were subjected to operation. In 4 cases the scope of the operation was purely exploratory, no attempt at removal being carried out. In 10 cases resection of the bowel was performed; 5 recovered from the operation, and 5 died as a result of it—a mortality and recovery rate of 50 per cent. each. Of the 5 cases that recovered 1 died of recurrence after forty-seven days. In 1 no data, beyond the fact of recovery, were attainable; 1 was well after six months; 1 after seven months; 1 after three years. The last case (Orth's) had been operated on five years previously for sarcoma of the ovaries; while the growth in the bowel may have been secondary to that in the pelvis, extirpated five years before, it is included here because of the length of time intervening, and because no other portion of the bowel was affected. In at least 4 of the 5 successful cases enlarged lymphatics were removed from the mesentery; and the fact that these cases recovered shows that the prognosis need not be bad on this account alone, and also the advisability of searching for and removing them.

**DIAGNOSIS.** The diagnosis of intestinal sarcoma, as of all intra-abdominal tumors, is a matter of much uncertainty. As Osler says, it is here that Bishop Butler's maxim that "probability is the rule of life" finds true application. Of 14 of our cases in which we have recorded the diagnosis made before operation or autopsy, in only 2 can the tumors be said to have been fairly accurately localized; in Bouilly's

case a diagnosis of malignant tumor of the intestine having been made, and in Orth's, one of mesenteric tumor. They were taken for tumors of the kidney, the omentum, the ovary, the peritoneum, the lymphatic glands, and in two cases they strongly simulated appendicitis—an observation of considerable importance. Again, the presence of metastasis to the lymph glands and the peritoneum may give rise to the presence of multiple tumors, which may be very confusing. We will briefly summarize the prominent symptoms presented in our cases, and then compare them with those offered by sarcoma of the small bowel and by carcinoma of the intestine.

The primary symptoms are gastro-intestinal manifestations of a dyspeptic type, especially abdominal pain, anorexia, and vomiting; progressive, rapid emaciation; moderate fever; abdominal distention, usually without ascites, but occasionally associated with œdema of the lower extremities; and the presence of a tumor, which is more often movable than immovable, frequently tender, usually of firm consistence, and often located in the right iliac region. The absence of obstruction in the great majority of cases is of great significance. The above chain of symptoms occur in persons of any age, but with greatest frequency in those under forty years, and with relative frequency in the early years of life. The group of symptoms cited does not differ materially from that associated with sarcoma of the small intestine, except, perhaps, the more frequent location of the tumor in the right iliac fossa in disease of the large intestine, owing to the frequent location in the cæcal region. The tumor may be very tender in the case of the large intestine, in which it probably does not differ from some cases of tumor of the small bowel, which in the majority of instances, however, are said to be slightly or not at all tender. Both are liable to be complicated by intussusception. König<sup>18</sup> believes invagination in intestinal tumors to be more common than is usually supposed, citing two cases in discussion.

Libman's statistics show that in the small intestine sarcoma may be found at all ages, although a large percentage of his cases were past thirty. A peculiar paleness or lividity of the complexion has also been described as rather characteristic of cases of sarcoma of the small intestine by both Baltzer and Libman. The differential diagnosis between this tumor of the intestine and carcinoma of the bowel, as well as between it and other intra-abdominal tumors, will, of course, arise. The first question is the only one we need refer to here. Baltzer laid stress on the age, sarcoma occurring earlier; the more rapid growth of sarcoma; the absence of obstruction, of marked tenderness, and of pain

during defecation; the early appearance of cachexia and the much greater prominence of general over local symptoms. Libman believes carcinoma of the bowel to be more common than Baltzer supposes in early life, but grants that under fifteen years the chances are in favor of sarcoma; he dwells on the absence of external glandular involvement, the absence of tenderness, and the large size of the growth in cases of sarcoma.

The main points of differentiation would seem to be in a sarcoma of the large bowel, its appearance in the majority of cases in early life (under forty), the early appearance, rapid growth, and large size of the tumor, the quick cachexia, and the absence of obstruction in most of the cases. Pain and tenderness may be present in both; but pain is an early and rather constant symptom in sarcoma of the large intestine, while in carcinoma it does not usually manifest itself until symptoms of obstruction develop.

PROGNOSIS AND TREATMENT. The prognosis without operation is, of course, bad. The life of the patient may be prolonged through a longer or shorter period of suffering, but medicinal treatment of specific nature remains to be discovered. Libman urges the use of arsenic where resection cannot be practised, calling attention to the fact that genuine cases of lymphosarcoma, usually multiple, or of the skin, have been cured by its exhibition, either internally or by injection. We know of no cases of intestinal sarcoma so relieved. The same is true of the use of Coley's fluid. On the other hand, operation, with resection of the growth, offers a fair chance for recovery in cases taken sufficiently early, the prognosis being at least as good, once the tumor can be safely removed, as in sarcoma elsewhere. It is contraindicated in cases far advanced in cachexia, which would be unable to stand the shock of operation, or where there is any other reason to believe that the widespread metastasis so characteristic of the later stages is present. In cases seen early, and in doubtful cases, exploratory laparotomy should be undertaken; 14 out of our 22 cases were operated upon. In 4 the operation was simply exploratory, no attempt being made to remove the tumor. In 10 cases resection was practised; 5 of these died as a result of the operation, either of shock or of peritonitis. Of the 5 that survived the operation, 1 died in forty-seven days of recurrence. Here, certainly, some metastatic growth had been present and not detected at operation. Of the remaining 4 all were living at the time of reporting. This was six months later in 1 case, seven months later in 1, three years in 1, and not stated in 1. In at least 4 of these 5 cases, as has already

been remarked, enlarged mesenteric glands were removed at the operation, showing that the presence of metastasis to the lymphatics is no contraindication to operation, and also the necessity of searching for these glands and removing them, if a radical operation is to be performed.

An operation attended with a mortality of 50 per cent. is a formidable one, and not to be lightly recommended; but when we consider the brief duration of life without it—about five and one-half months being the average in the cases not operated upon—and the fairly good results in cases which survive resection, the operation, it would appear, should be advised when thorough removal seems feasible or likely. The section of the bowel should be made through a healthy area, well to each side of the microscopically diseased portion, in order to get beyond the infiltrating cells spreading, sheet-like, in the submucosa and subserosa. When, on opening the peritoneal cavity, the lymphatics and peritoneum are found extensively involved, and the liver and kidneys large on palpation—and, perhaps, nodular—simple closure of the wound will be all that can be done unless obstruction be present, when the formation of an artificial anus above the stenosed area would be indicated.

Van Zwahlenberg,<sup>10</sup> in a study of 15 cases of resection of the bowel in various regions for sarcoma, found 9 recoveries and 6 deaths. Children stood operation very well. Of 5 cases under ten years of age only 1 died.

In preparing our list of cases we have excluded those reported by Perceval,<sup>19</sup> W. S. Thorne,<sup>20</sup> and Djemil-Pacha.<sup>21</sup> In Perceval's case the nature of the tumor is too uncertain to classify it; in Thorne's, from the histological examination, the tumor was probably a carcinoma, and in Djemil-Pacha's case, one of sarcoma of the great omentum and transverse colon, the tumor was probably primary in the omentum.



TABLE OF CASES.

Reporter.	Sex and age.	Variety.	Location.	Duration.	Metastasis.	Operation.	Remarks.
1. H. Arpott, Traus. Path. Soc. London, 1874, xxv.	M. 4 yrs.	Lympho-sarcoma (lymphoma).	Transverse colon.	A little over 2 months.	Mesenteric glands, kidney, liver, epididymis, spermatic cord, skin of abdomen.	None.	Died from purulent peritonitis.
2. W. Horn, Hamburg, 1882, quoted by Orth, loc. cit.	F. youth.	Spindle-cell sarcoma.	Descending colon; stenosis of gut.	Unknown; no symptoms before obstruction developed.	Not stated.	None.	Death from acute intestinal obstruction due to stenosis of intestine.
3. A. Debrunner, Inaug. Dissert., Zurich, 1883, quoted by Orth	M. 5 yrs.	Round-cell sarcoma.	Transverse colon.	About 7 weeks.	To omentum, whole abdominal cavity seem'd filled with white or pale red tumors.	None.	Death from exhaustion.
4. A. Debrunner, loc. cit.	F. 16 yrs.	Round-cell sarcoma.	Sigmoid flexure. Some stenosis.	4 months.	Retroperitoneal glands, left ovary, apex of left lung.	None.	Death from peritonitis.
5. H. Beck, Zeitschr. f. Heilkunde, 1884, v. p. 442.	F. 59 yrs.	Lympho-sarcoma.	Cæcum and ileum	Not stated.	Cervical lymph glands, both lungs, encroaching on pleura and pericardium, spleen, stomach, ileum, and mesenteric glands.	None.	Diagnosed lymphoma of cervical and abdominal lymphatic glands death from heart failure.
6. F. Lange, New York Med. Journ., 1886, xliii. p. 199.	F. 32 yrs.	Not stated.	Transverse colon.	Uncertain.	Omentum, mesenteric glands, both ovaries.	Resection of bowel, removal of ovarian tumors.	Primary seat doubtful; possibly in ovary. Death from septic peritonitis on ninth day; leakage probably from incessant vomiting.
7. Bouilly, Bull. et Mém. de la Soc. de Chir. de Paris, 1888, n. s., xiv. p. 601.	F. 44 yrs.	Lympho-sarcoma.	Cæcum and ileum.	Symptoms for 5 years; tumor for 8 months.	Lymphatic glands in mesentery.	Resection.	Recovered; well seven months later.
8. L. Orth, Inaug. Dissert., Heidelberg, 1890, "Ueber die Sarkome des Darms, Mesenteriums u. Retroperitonealen Raums."	F. 34 yrs.	Lympho-sarcoma (alveolar)	Transverse colon.	3 months.	Lymphatic glands of mesentery.	Resection (Czerny).	Had ovaries removed for sarcoma five years before; living and well three years later.
9. R. v. Baracz, Arch. f. klin. Chirurg., 1891, xlii. p. 501.	M. 8 yrs.	Round-cell sarcoma.	Cæcum; tumor formed apex of ileo-cæcal intussusception.	13 weeks.	A nodule in neighborh'd of ileo-cæcal valve.	Lumbar incision; resection of tumor and intussusception.	Diagnosis malignant growth in a movable left kidney or in descending colon. Death from shock second day.
10. E. Becker, Deutsche Zeit. f. Chirurgie, 1894, xxxix.	M. 35 yrs.	Round-cell sarcoma.	Cæcum.	5 weeks before operation; lived 47 dys. after operation.	Not stated.	Resection.	Recovery from operation; death from recurrence.



Reporter.	Sex and age.	Variety.	Location.	Duration.	Metastasis.	Operation.	Remarks.
11. H. R. Wharton, International Clinics, 1894, 4th series, ii, p. 199.	F. under 2 yrs.	Round-cell.	Cæcum.	Sick several weeks before admission; still alive several months later.	To orbit.	Exploratory; portion removed for examination.	Symptoms simulated appendicitis before operation; when reported tumor was growing and orbital sarcoma had developed. Resembled acute appendicitis at onset; died of cachexia about six weeks after operation.
12. H. R. Wharton, personal communication.	M. 21 yrs.	Round-cell.	Cæcum.	About two months.	To peritoneum.	Exploratory.	Death from shock 36 hrs. after operation.
13. R. Abbe, Annals of Surgery, 1895, xxi, p. 592.	M. 6 yrs.	Not stated; no micros. exam'n.	Cæcum and ascending colon.	Symptoms for 1 week.	Mesenteric glands.	Resection.	Death 2 days after operation.
14. C. Levi, Bull. de la Soc. Anat. d. Paris, 1890, lxx, p. 68.	F. 38 yrs.	Round-cell.	Sigmoid flexure.	2 months.	None.	Excision Tuffier; formation of artificial anus; true nature not diag. until removed.	Death 2 days after operation; fatty liver, weighing 3200 grammes.
15. F. Smoler, Prager med. Woch., 1898, xxiii, p. 145.	M. 27 yrs.	Lympho-sarcoma.	Cæcum, ileum, and ascending colon.	Not stated.	Mesenteric glands.	Resection.	Death 2 days after operation, from septic peritonitis.
16. F. Smoler, loc. cit.	M. 19 yrs.	Lympho-sarcoma.	Cæcum and ileum.	Not stated.	Peritoneum.	None.	
17. Blauel, Virch. Archiv, 1900, clxii, p. 487.	M. 33 yrs.	Round-cell.	Cæcum and ascending colon.	18 months.	Retroperitoneal and portal lymph glands.	Tum. punctured, later incised and drained; opening communicated thro' tum. cavity with bowel.	Colon bacillus found in fluid evacuated. Death from exhaustion 4 days after opening.
18. Blauel, loc. cit.	F. 66 yrs.	Round-cell.	Cæcum.	7 months.	Mesenteric and retroperitoneal glands and liver.	Exploratory.	Died 25 days after operation, anastomosis between tumor cavity and two loops of small intestine resembled tuberculous condition. Purpura hemorrhagica; infection by bacillus probably B. aerogenes capsulatus.
19. T. Fisher, Bristol Med.-Chir. Journ., 1901, p. 29.	M. 28 yrs.	Lympho-sarcoma.	Cæcum and ileum.	3½ weeks.	Few small subperitoneal growths in mesentery.	None.	Recovery, 6 mo. later was well; mother and paternal grandmother died of sarcoma.
20. C. Van Zwalenberg, Journ. Amer. Med. Assoc., March 9, 1901.	M. 5 yrs.	Lympho-sarcoma.	Cæcum; partial intussusception of ileum and vermiform into cæcum.	5 months.	Mesenteric glands and ileum.	Resection.	Recovery.
21. Hofmokl, quoted by Van Zwalenberg.	F. 24 yrs.	Lympho-sarcoma (adenosarcoma).	Cæcum.	Not stated.	Not stated.	Resection.	Recovery.
22. Jopson and White.	M. 4 yrs.	Round-cell.	Cæcum and ascending colon.	Probably nine or ten months.	Mesenteric glands, peritoneum, kidney, spleen, and liver.	None.	Liver large and fatty, with some tumor infiltration.

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## A CASE OF COMPLETE ABSENCE OF THE VISUAL SYSTEM IN AN ADULT.<sup>1</sup>

By WILLIAM G. SPILLER, M.D.

[Read November 6, 1901.]

COMPLETE absence of the visual system is of very rare occurrence, especially in an adult. The study of the case I report in this paper should be of more value than one of agnesia of the visual system in a newborn child, because in the latter portions of the brain not belonging to the visual system are imperfectly developed, and faulty conclusions may therefore be drawn.

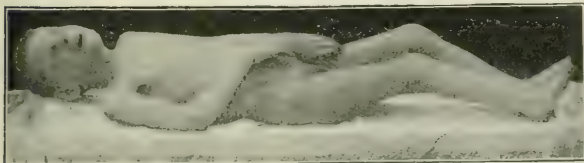
The boy, T. S., according to the case-books of the Pennsylvania Training School for Feeble-minded Children, was born in 1878, and was admitted to the School March 12, 1895. At the time of admission he weighed thirty-eight pounds, and his height was three feet seven inches. He was an idiot, absolutely helpless, and very unclean. He could say "mamma," and nothing more. He was passionately fond of music. At the time of admission to the school he appeared to be about eight or ten years of age.

I saw him on July 30, 1897, and made a few notes on his condition. I regarded the case at that time as one of cerebral spastic paraplegia of the lower limbs, with absence of the eyeballs. The boy was unable to stand alone, and if he were stood up and not supported he fell backward. When supported he could take a few steps, but in so doing one lower limb was moved in front of the other (crossed-leg progression). His knee-jerks were exaggerated, but ankle clonus was not obtained. He could move his lower limbs while he was sitting, and there was not excessive rigidity of these limbs on passive motion. He uttered only a few monosyllables. His palpebral fissures were very small. He died March 2, 1900, and the necropsy was made two days later. The necropsical notes I shall use only in so far as they are of importance for the understanding of the case.

<sup>1</sup> From the William Pepper Clinical Laboratory (Phoebe A. Hearst Foundation).

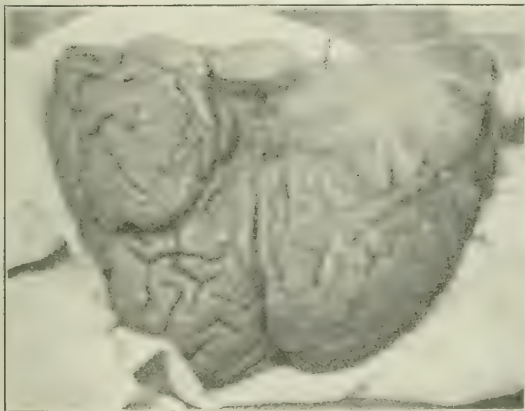
The body was that of a child apparently about twelve years of age (see Fig. 1), though in reality his age was twenty-two years. No signs of pu-

FIG. 1.



A photograph of T. S., taken after death. The right upper limb, the fingers of both hands, and the lower limbs are slightly contractured. The palpebral fissures are small.

FIG. 2

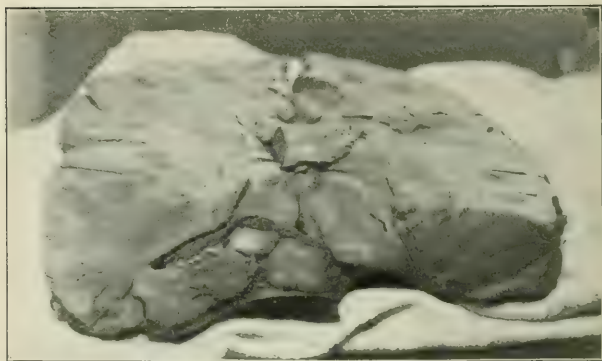


The occipital lobes have been cut away. A portion of the right temporal lobe has also been cut away in order to show the complete absence of the visual system. The internal geniculate body (A) is well shown, but no trace of the external geniculate body or of an optic tract or chiasm can be found.

erty were present. The testicles were not in the scrotum; the right testicle, quite small, was found in the inguinal canal just above the pubes. The

genitalia were like those of a child of ten years. No hairs were found on the pubes, or in the axillæ, or on the face. The circumference of the head was eighteen and three-fourth inches; the length of the body was forty-seven inches. The right upper limb could not be fully extended at the elbow, while the left upper limb could be fully extended. Slight contracture of the fingers of each hand was observed, so that the fingers could not be fully extended when the hands were fully extended at the wrists. The fingers could be fully extended when the hands were flexed at the wrists, as the contracture of the flexors of the fingers did not then interfere with the extension of the fingers. The lower limbs were slightly flexed at the knees, and could not be fully extended.

FIG. 3.



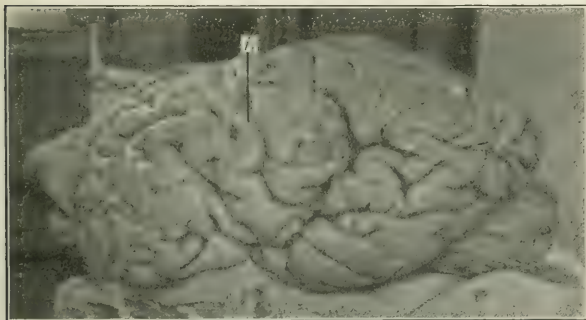
The optic thalami are well shown. The anterior colliculi of the corpora quadrigemina, especially the right colliculus, appear smaller than the posterior, because the former were further from the camera.

The palpebral fissure of each eye was very small, and the orbits contained only a small amount of what appeared to be fibrous connective tissue. Unfortunately, permission had not been given for the removal of the orbital contents. Nothing resembling an eyeball was seen.

The optic foramina did not exist, and it was impossible to find an opening in the usual situation of these foramina, and here there were merely slight depressions in the skull. No trace of optic nerves, chiasm, or optic tracts could be found. (See Fig. 2.) There was no sign of an external geniculate body on either side, and the thalamus on each side had nothing

resembling an optic tract passing from it. The posterior part of each thalamus was rounded and larger perhaps than one would expect to find it in a case of complete agenesia of the visual system. (See Fig. 3.) The brain was small, firm, and not cedematous. The left ascending

FIG. 4.



The left ascending frontal convolution in the centre for the upper limb (B) is very narrow.

FIG. 5.



The upper part of the right cerebral hemisphere, showing the small cuneus C.

frontal convolution in the centre for the upper limb was very small (see Fig. 4), to which fact possibly was due the contracture of the right forearm (see Fig. 1), because of imperfect development of the nerve fibres innervating this limb. The anterior colliculi of the corpora quadrigemina were

fully as large and as well-developed as the posterior. The occipital lobes were small, and the cuneus on each side (see Fig. 5) was small and the calcarine fissure short. The lower olives were covered by thick bands of nerve fibres—*i. e.*, the external arcuate fibres were unusually well-developed.

The spinal cord was small, but not otherwise abnormal.

The brain was hardened in formaline, and the basal ganglia of one hemisphere were cut in serial sections, while those of the other hemisphere were

FIG. 6.



Photograph of a horizontal section of one cerebral hemisphere, showing Meynert's commissure (B) well developed, and also the internal geniculate body (C), while the external geniculate body is entirely absent

preserved intact as a gross specimen. Sections were made through the cortex of the left calcarine fissure, and stained by thionin and by Weigert's hæmatoxylin method. Frontal sections were made through the right occipital lobe in order that the optic radiations might be studied when cut transversely. The nerves supplying the ocular muscles were also cut and examined.



The cortex of the left calcarine fissure stained by thionin contained many nerve-cell bodies, but they were possibly slightly less numerous than are the cell bodies in sections from the corresponding region of a normal brain, especially in the third, fourth, and fifth layers. The giant cells of the third layer were represented, but were possibly not so numerous as in a normal brain. The fibres of Vicq d'Azyr of the cortex of the calcarine fissure were not very distinct in sections stained by Weigert's hæmatoxylin method, but they were not entirely absent.

The optic radiations in the frontal sections of the occipital lobe were not entirely absent, but the area occupied by them was not very distinct.

Meynert's commissure was normal, and stained well by Weigert's hæmatoxylin method. (See Fig. 6.)

Careful examination of the serial sections failed to show the slightest trace of an external geniculate body on either side, although the internal geniculate body was well developed. Fig. 6, a photograph from one of the sections, shows the internal geniculate body in its normal size, as well as the inferior posterior portion of the optic thalamus, but the external geniculate body, which should be present in a section at this level, is entirely absent. Comparison with Fig. 326 of the *Anatomie des Centres Nerveux*, vol. i., by J. and A. Dejerine, is instructive. This drawing is from a section cut in the same direction as that represented in Fig. 6 of my series, and shows the normal size of the external geniculate body and an optic tract in a section from this level. In the section of my series represented in Fig. 6 there is no trace of an optic tract.

Some few medullated nerve fibres are found within the pulvinar in my section, but those in the posterior portion of the thalamus are much fewer than those in the more anterior portions. The contrast is very striking, and is represented in a drawing of a horizontal section (see Fig. 7), which should be compared with a corresponding section from a normal brain, as shown in Fig. 321 of the *Anatomie des Centres Nerveux*, by J. and A. Dejerine.

The habenula in the horizontal sections appears well developed, and the fasciculus retroflexus of Meynert is well stained.

In the photograph the anterior colliculi of the corpora quadrigemina appear smaller than the posterior; but this is merely because the former were further from the camera.

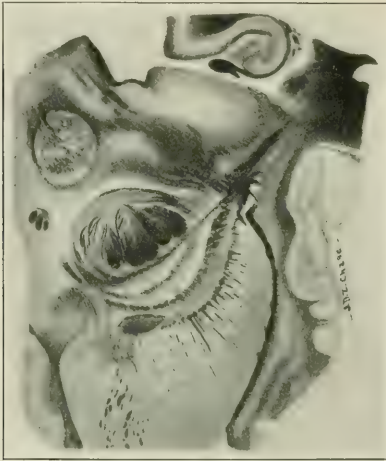
Sections through one half of the oculomotor nuclei stained with thionin contain many nerve-cell bodies belonging to these nuclei, and these cell bodies stain well with thionin and appear to be normal. They are possibly not as numerous as cell bodies in oculomotor nuclei of a normal brain. Sections through one-half of the oculomotor nuclei were also stained by the Weigert hæmatoxylin method.

Transverse sections of the extracerebral portion of the left oculomotor nerve near the cerebral peduncles stained with ammonium carmine show an

apparently normal nerve. The nerve is possibly smaller than an oculomotor nerve from a normal brain, but it contains no sclerotic areas. It contains, however, some areas in which very fine nerve fibres form distinct groups, but there is no scarcity of large nerve fibres.

Transverse sections of the right oculomotor nerve are very similar to those of the left oculomotor nerve. The sections stain well by Weigert's hæmatoxylin method.

FIG. 7.



A drawing of a horizontal section through the basal ganglia of one hemisphere. The fibres entering the posterior part of the optic thalamus are few in number.

One of the trochlear nerves in transverse sections, stained either by ammonium carmine or Weigert's hæmatoxylin, appears to be normal, and contains nerve fibres of good size. The nerve fibres stain well with the Weigert hæmatoxylin, but in sections so stained the nerve fibres are perhaps not quite so close together as in the trochlear nerve from a normal brain.

The nerve fibres of the left abducent nerve stained in transverse sections by acid fuchsin are exceedingly small, much smaller than those of the oculomotor and trochlear nerves, but they stain well with Weigert's hæmatoxylin.

The right abducent nerve in transverse sections stained by acid fuchsin contains many nerve fibres that are much larger than any of those found in

the left abducent nerve, but it contains also many sclerotic areas. Some of the nerve bundles stained by Weigert's hæmatoxylin method contain very

FIG. 8



Drawings of transverse sections through portions of the abducent nerves. The upper drawing represents the fine fibres of the left abducent nerve, and the lower drawing the sclerotic areas in the right abducent nerve.

few medullated nerve fibres. The contrast between the abducent nerves and the other two ocular nerves on each side is most striking. (See Fig. 8.)

The nucleus of each abducent nerve contains many nerve-cell bodies, which, with the thionin stain, appear to be normal.

The nerve-cell bodies of the anterior horns of the spinal cord in the cervical and lumbar regions stained with thionin are normal, but possibly a little smaller than those usually present in the anterior horns. No sclerotic areas are found in the lateral columns, neither are the nerve fibres in these columns unusually fine in transverse sections.

Von Monakow gives as primary optic centres the external geniculate body, the surface of the pulvinar, and the superficial gray matter of the anterior colliculi of the corpora quadrigemina. He says that Stilling, Bernheimer, and Kölliker believed that visual fibres arise also in the subthalamie body, the internal geniculate body, and the tuber cinereum. The anterior colliculi of the corpora quadrigemina in man, according to his view, have a very subordinate rôle in vision, and he believes that about 80 per cent. of the optic nerve fibres terminate in the external geniculate body. My case of congenital absence of the central visual system confirms these views of von Monakow. It shows also that Meynert's commissure and the habenula are not part of the visual system. According to von Monakow (*Gehirnpathologie*), centrifugal fibres—i. e., fibres having their origin in the visual cortex—are present in the optic radiations and pass to the inter-brain and mid-brain. The giant pyramidal cell bodies of the third layer in the cortex of the occipital lobe give off axones, which pass by way of the optic radiations and the arm of the anterior colliculus of the corpora quadrigemina, to terminate in the superficial medullary substance and gray matter about the aqueduct of Sylvius in the anterior colliculus. The Vicq d'Azyr fibres, he says, are often in a double row in the occipital lobe. They come, in greater part, from the fibres of the optic radiations which pass to the third layer of the cortex, but some of the Vicq d'Azyr fibres may belong to an association system. In long-standing lesions of the optic radiations the Vicq d'Azyr fibres are very atrophic, and the double row of these fibres is scarcely recognizable. In my sections the comparatively few fibres passing to the pulvinar are doubtless the fibres described by von Monakow as arising in the occipital lobe, and in my sections the Vicq d'Azyr fibres are not very distinct.

Von Leonowa has examined the microscopical sections from four cases of anophthalmia and three cases of atrophy of the eyeball, but in all these death occurred within a few months after birth. In all her cases the posterior colliculi of the corpora quadrigemina were intact, but the anterior colliculi were affected. Von Leonowa<sup>1</sup> concludes from a study of the cases mentioned above that the posterior colliculi of the corpora quadrigemina have no relation to vision, while the anterior have; that the relation of the external geniculate body to the visual fibres is a very intimate one; and that the sub-thalamic body has no relation to vision. In none of her cases was the absence of the visual system complete, and all the brains were from children in the early periods of extra-uterine life.

In her cases the nuclei of the third, fourth, and sixth cranial nerves were intact, and this integrity is explained by von Leonowa as a consequence of the existence of ocular muscles. The external ocular muscles may be well-developed, even though the eyeballs are exceedingly atrophic, as in a case of anophthalmia in a person of twenty-seven years, reported by Haab, in whom the ocular muscles were normal in size and shape, although the ocular bulbs were very small. The nerves to the ocular muscles need not be absent in congenital defect of the visual system. In my case there was apparently no eyeball on either side, but in the small amount of fibrous tissue at the posterior portion of each orbit muscles may have existed, even though they had little or no function. One might suppose that in the case I have reported the third, fourth, and sixth nerves would have been very imperfectly developed in conformity with the law of Gudden, according to which atrophy in a neurone follows injury to this neurone. It should be remembered, however, that in my case the ocular nerves were not injured, and may have been in union with ocular muscles, as in Haab's case.

It has been shown by von Leonowa<sup>2</sup> in the report of a much-quoted case that nerve fibres may develop, although they apparently have no function. She examined a fœtus in which the brain and spinal cord had not developed, and yet the vertebral canal was filled in its entire extent by posterior nerve roots. Some of the fibres of the

<sup>1</sup> Archiv für Psychiatrie, 1896, vol. xxviii, p. 53.

<sup>2</sup> Neurologisches Centralblatt, 1893.

posterior roots extended from the lower part of the canal to the upper, as they would have done if they had formed the posterior columns of a normal spinal cord. All the posterior roots ended blindly, and appeared as though they had sought a spinal cord in which to bury themselves. No anterior roots were found. All the peripheral nerve fibres present had their origin in the spinal ganglia, and belonged, therefore, to the sensory system. The muscles of the limbs appeared fully normal, although no motor nerves existed. Most of the axis-cylinders of the posterior roots were non-medullated or had only a thin medullary sheath. The cell bodies of the spinal ganglia were as numerous and as well-developed as in a normal foetus. The absence of medullary sheaths on the posterior roots, von Leonowa thinks, may have been caused by the amniotic fluid, inasmuch as medullary sheaths were present on axones that were covered by the skin.

Gade<sup>1</sup> and Karl and Gustaf Petrén have found posterior roots growing into the spinal canal in complete failure of development of the spinal cord. I am unable to determine from the statements of the latter authors whether in their case or in Gade's the individual fibres of the posterior roots were normal or not.

With the results of these investigations in mind we can understand that nerves might grow equally well into the orbits and persist, even though the ocular muscles were absent. Indeed, von Leonowa and Karl and Gustaf Petrén have shown also that in early life muscles may be developed, although no motor nerves exist, so that the converse may well be true—*i. e.*, motor nerves probably may exist, although the muscles usually supplied by these nerves are not developed. All the ocular nerves in my case, however, were not normal. The two sixth nerves were very imperfectly formed.

Meynert's fibres are asserted by some to be the connection between the optic nerves and the oculomotor centres, although such distinguished cerebral anatomists as Edinger and von Monakow tell us that the anatomical proof for this assertion is wanting. Recent investigations seem to indicate that some of *these* Meynert fibres (for there is more than one band of fibres named after Meynert)

<sup>1</sup> Gade, cited by Karl and Gustaf Petrén. Virchow's Archiv, 1898, B. 151.

belong to a bundle extending into the anterior column of the spinal cord. In my case the Meynert fibres in the corpora quadrigemina were well developed, although there could have been no reflex fibres from the iris to the oculomotor centres, so that we must conclude that the function of these Meynert fibres cannot be merely to serve the pupillary reflex. I am unable to give the course of the so-called pupillary fibres from a study of my preparations, as the fibres in the region of the corpora quadrigemina form an intricate network.

It is not surprising that cell bodies should be numerous in the cortex of the calcarine fissure in a case of congenital absence of the visual system. Some of these cell bodies have axones which are situated in the optic radiations and terminate in the primary optic centres—*i. e.*, the external geniculate body, the pulvinar of the thalamus, and to a less extent the anterior colliculi of the quadrigeminal bodies, and these fibres probably are not directly concerned in vision. The visual cortex is intimately connected with widely separated portions of the brain, as shown both by physiological and anatomical investigations. The movements of the limbs, the functions of speech, and especially the movements of the eyeballs, are in intimate relation with vision, and important association tracts between the visual area and other parts of the brain can be demonstrated anatomically. The cell bodies of the visual cortex must have axones in relation with remote parts of the cerebral cortex, and, therefore, it is not surprising that these association neurones are developed even in a case of congenital defect of the visual system. Von Monakow represents in his *Gehirnpathologie* (p. 265) a section of a calcarine cortex from a case of lesion of the optic radiations. The giant pyramidal cell bodies of the third layer of the cortex had entirely disappeared, and the third, fourth, and fifth layers were degenerated in a way they were not in my case. It should be remembered that in von Monakow's case the axones destroyed were those of cell bodies situated in the calcarine cortex, and that atrophy of these cell bodies probably followed the injury of their axones. This did not occur in my case, and probably the nerve fibres present in my specimens in the optic radiations arose in the occipital lobe. It is difficult to understand what the function of these fibres can be.



Although the individual described in this paper was an idiot, we should be cautious in attributing his deficient mental development to the absence of his visual system. It would seem probable, however, that the entire brain was in a state of imperfect development.

The spastic paraplegia of the lower limbs deserves mention. The nerve-cell bodies of the anterior horns in the lumbar cord were normal by the thionin stain, except that they were not so large as the cell bodies of this region usually are, and the lateral columns did not contain sclerotic areas. This is not the first time I have found an apparently normal spinal cord in congenital spastic paraplegia, and I think the explanation is to be found in an imperfect development of the motor neurones. A deficiency from birth in the number of these neurones would probably have the same result as partial destruction of the central motor tracts, and in the absence of the development of motor neurones there would be no sclerosis, inasmuch as no space existed to be filled by proliferation of the neuroglia. Indeed, sclerosis may be entirely absent if destruction of nerve fibres occurs in early life, because the growing tissue of the spinal cord fills the space left by degenerated fibres, and proliferation of the neuroglia does not occur. I have seen the spinal cord in a case of infantile hemiplegia presenting little or no sclerosis, although the person from whom this cord was removed had lived many years after the paralysis had developed. The case to which I refer was in Dejerine's service. In two cases of congenital spastic paraplegia of the lower limbs I believed I was able to detect an unusual fineness of the nerve fibres of the pyramidal tracts, but I was unable to do so in this case (T. S.).

I am indebted to Dr. de Schweinitz for the reference to a case reported by W. S. Little<sup>1</sup> in 1885, in which congenital absence of some portions of the visual system was found. The brain was from a child of ten years of age, who had been an inmate of the Pennsylvania Training School for Feeble-minded Children, and the specimen was examined by A. W. Wilmarth. This child had had bitemporal hemianopsia. There was no optic commissure, but a small projection was found on the inner side of each nerve where the commissure should have been. These projections did not touch by at least one-

<sup>1</sup> Transactions of the American Ophthalmological Society, 1885, p. 367.

quarter of an inch. A complete study of the specimen does not seem to have been made.

A still more important case, and one more closely resembling mine, has been reported by Haab.<sup>1</sup> His specimen was from a girl, twenty-seven years old, who had the development of a child of fourteen or fifteen years, and from her appearance had not reached puberty. She was an idiot, and had much difficulty in walking. The optic chiasm was entirely absent, but the optic tracts were present as small bands. The oculomotorius, abducens, and trochlearis appeared to be normal, and yet the merest trace of an eyeball was found. The muscles of the orbits appeared to be normal. The external geniculate body was entirely absent, but the internal geniculate body was of normal size. The corpora quadrigemina were of normal size macroscopically. The optic foramen was almost obliterated. The pulvinar of the optic thalamus was smaller than in a normal brain.

The conclusions that may be drawn from my case are :

1. The chief "primary" optic centre is the external geniculate body.
2. The pulvinar of the optic thalamus is also an important "primary" optic centre.
3. The anterior colliculus of the quadrigeminal body in man has an unimportant relation to vision.
4. The subthalamic body, the habenula, the internal geniculate body probably are not part of the visual system.
5. The cortex of the calcarine fissure may contain nearly the normal number of cell bodies, even though the visual system may be undeveloped.
6. The nerves to the ocular muscles and their nuclei may be developed, even though the visual system is absent.
7. Congenital spastic paraplegia may be the result of deficient formation as regards number or size of the neurones of the central motor system, even though such a deficiency may be difficult to detect by the microscope.

<sup>1</sup> Beiträge zur Ophthalmologie als Festgabe Friedrich Horner, 1881, p. 131.

## THE RELATION OF TUBERCULOSIS TO PSEUDOLEUKÆMIA.<sup>1</sup>

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[Read November 6, 1901.]

THE etiology of Hodgkin's disease, or malignant lymphoma, is one of the most elusive problems in medicine; in fact, there are now included under this term a number of conditions, most of which are struggling with slight success for recognition as disease entities. That certain of the cases are due to a peculiar form of tuberculosis of the lymphatic apparatus has been recognized for a considerable time, chiefly as a result of the brilliant article of Sternberg; but such cases have been considered rather as pathological curiosities than as clinically recognizable. The majority of cases have been diagnosed pseudoleukæmia, and only the autopsy has revealed the true condition. Indeed, it has required an histological examination and even careful inoculation experiments (Brentano and Tangl, Sabrazès) before the etiology was clear. In some cases (Freudenweiler, Kosler) tuberculosis of some of the other organs has been recognized as a complication, but has not been supposed to be the cause of the pseudoleukæmic manifestations.

I have, in a comparatively brief period, had the opportunity of

<sup>1</sup> Before reading his paper Dr. Sailer stated that his reason for employing the term "Sternberg's Disease" was that he had found in Sternberg's article, published in 1898, the first systematic and careful attempt to determine, by extensive studies, the relation between tuberculosis and the syndrome of pseudoleukæmia. Sternberg proved that this relation was very definite and close, and that in many cases previously considered to be true instances of pseudoleukæmia it was justifiable, from the histological findings, to make a diagnosis of tuberculous infection of the glands.

observing four cases of the tuberculous form of pseudoleukæmia, in all of which autopsies were obtained, and all presenting certain common clinical features.

CASE I.—M. S., male, white, single, an Austrian by birth, and launderer by occupation, was admitted to the wards of Dr. William E. Hughes at the Philadelphia Hospital, April 4, 1901. As he spoke only Polish, a history was obtained with great difficulty. Through an interpreter it was learned that his father and one sister had died of some unknown cause. His mother had died of pneumonia after having been sick for seven days; another sister had died at the age of four.

His present sickness commenced four months before admission, the first symptom being a severe cough, with expectoration, followed by progressive weakness and loss of weight. A month later he suffered from pain in the abdomen and back, which at times was sharp. He was constantly thirsty, but drinking water increased the pain. He also had had chills. For three months he had been on an absolute milk diet. He stated that he had not noticed any enlargement of the abdomen, nor any change in the character of the urine.

When admitted it was noted that he was a fairly well-developed man. His tongue was moist and slightly coated in the centre. The pulse was regular, rapid, full, and of good force. The peripheral arteries were slightly sclerosed. The pupils reacted normally; the muscles of the eyes were normal, and the mucous membranes were pale. The thorax was slightly flattened; the abdomen bulged slightly in the upper part, especially on the right side. The left lung was normal. The right lung anteriorly showed dulness at the apex, gradually diminishing toward the base to a normal note. The respiratory sounds were harsh, especially at the apex. Posteriorly there was also dulness at the apex, diminishing toward the base; some crepitation heard everywhere, and moist, almost bubbling, râles at the apex.

The heart was normal. The liver could be distinctly palpated, extending a hand-breadth below the costal margin. Its surface was smooth. Pressure caused pain. The extremities were negative.

April 5th the following notes were made. There is a profuse expectoration streaked with blood; the eyes are sunken; the skin is an olive color. The right side of the thorax moves less than the left during respiration. Tactile fremitus and vocal resonance are greatly increased at the right apex, and there are numerous crackling râles. The liver extends from the fifth rib to two inches below the costal margin, and is quite tender. The spleen is greatly enlarged and extends six inches below the costal margin. The sputum was examined, and diplococci and staphylococci were found, but no tubercle bacilli. The urine was red, the specific gravity 1026, a considerable amount of albumin was present, and there were numerous red

blood cells in the sediment. The blood showed: Haemoglobin, 47 per cent.; red blood cells, 4,010,000; white blood cells, 6000.

*April 6th.* The blood examination gave: Haemoglobin, 50 per cent.; red blood cells, 3,050,000; white blood cells, 7200; polymorphonuclear, 63 per cent.; transitional, 15 per cent.; mononuclear, 17 per cent.; eosinophile, 5 per cent.

*7th.* The urine contained albumin in considerable quantity and blood casts. Specific gravity, 1022.

*10th.* The patient is stronger and out of bed; he is greatly emaciated, his expression is dull and he complains of pain at the apices of both lungs. The sputum is copious and rusty, but does not contain tubercle bacilli.

*11th.* Patient complains of great weakness.

*12th.* A very few tubercle bacilli are found in the sputum for the first time. The patient is weaker than yesterday, and complains of great tenderness in the region of the liver.

*27th.* The liver and spleen are increasing in size; there is movable dullness in the flanks and fluctuations in the abdomen. The sputum contains numerous tubercle bacilli.

*29th.* The ascites has increased enormously, and it is impossible to palpate the liver and spleen. There is no dyspnoea, but the respirations are very slow (12 to 16). (Edema of the lungs developed rapidly, and the patient died at 8.30 P.M.

During the stay of the patient in the hospital I had opportunity, through the kindness of Dr. Hughes, to demonstrate the case repeatedly to my ward classes. The diagnosis that at first seemed most likely was pseudoleukæmia. Afterward, when the nature of the process in the lungs was recognized, it was changed to pulmonary tuberculosis with amyloid disease, although later I regarded the case as pseudoleukæmia associated with the lung conditions. I was not at this time thoroughly familiar with Sternberg's article.

The autopsy was performed April 30, 1901, at 12.30 P.M., by Dr. F. J. Kaltefleiter. The pathological diagnosis was as follows: Tuberculosis of the lungs; chronic pleurisy with adhesions; cirrhosis of the liver; congestion of the spleen and kidneys; tuberculosis of the intestines, and ascites. I quote the following from the notes:

"The peritoneal cavity contained 2500 c.cm. of straw-colored fluid; specific gravity, 1015. The lower margin of the liver extended 3 cm. below the costal margin. The heart was normal. The left lung was studded with miliary tubercles from the apex to the base. The right lung was densely studded with tubercles, varying in size, the larger ones 3 to 4 mm. in diameter, and usually caseous in the centre. The spleen was greatly enlarged measuring 18 x 13.5 x 3.5 cm. It weighed 680 grms. The capsule was thickened and the tissue congested. The kidneys were large, dark, and friable, but showed no gross lesions. The liver was enlarged, measuring

26 x 21 x 6.5 cm., and weighing 1990 grms. It was granular, firm, and contained numerous yellow tubercles surrounded by yellowish-red liver substance. The small and large intestines contained a number of tubercular ulcers of various sizes. The tissues were unfortunately lost, and microscopical studies could not be made."

CASE II. —G. G., a negro, aged twenty-eight years, a driver by occupation, was admitted to Dr. Musser's wards at the University Hospital on May 24, 1901. He had always worked hard, and his appetite had been good; he indulged moderately in alcohol and used tobacco to excess. His mother had died at the age of eighty; his father is living and well at the age of seventy. One sister died at the age of eighteen from a "bad cold;" one sister and three brothers are living and well so far as he knew. There was no history of tuberculosis, and only an indefinite history of tumor in an aunt.

Up to the time of the beginning of his sickness he had always been well and exceptionally strong. About five years ago he had had an attack of pain in the right hip; he had never had any venereal disease, nor any of the ordinary diseases of childhood. Two years ago, while lifting a barrel of oysters, he had felt a sensation of something giving way in the sternum, and two days later a tumor appeared near the xiphoid, which grew rapidly for a month, and then remained stationary in size. It had never been painful, and had never given him any trouble whatever. A few days later he noticed that the right side of the abdomen was full, and he felt a mass there which he supposed was a tumor. This also had never been painful nor given him any discomfort. About a month before admission he noticed some pain in the back and hip, and some swelling of the feet, particularly at night. He also had a cough, with expectoration, and the day before admission profuse nose-bleed. On two occasions he had had night-sweats, and felt feverish for several days. His physical condition was as follows:

The arteries pulsated vigorously. The superficial lymph glands were not enlarged. A hemispherical tumor covered the lower part of the sternum, extending from the level of the fourth interspace to below the xiphoid cartilage, and from 2 inches to the left to 1.5 inches to the right of the sternum. It fluctuated, but did not pulsate, and was not affected by respiration or cough. It could not be reduced by pressure; it was neither painful nor tender. It was surrounded by a zone of absolute dulness about one-half inch broad. The upper portion of the thorax was fuller on the right than on the left side, and moved more during respiration. The percussion note was slightly impaired at the right apex. Tactile fremitus and local resonance were increased at this place, and there was slight pectoriloquy. Inspiration was slightly harsh and interrupted synchronously with the heart-beat; expiration was harsh and as long as inspiration. The left lung was normal. Posteriorly the respiratory sounds were vesicular; more distinct on the left than on the right side. There was a distinct cardiac impulse over the

præcordium. The apex-beat was in the fifth interspace, inside the nipple line, powerful and diffuse. The area of cardiac dulness was bounded by the fifth rib and the nipple line, and merged into the dulness of the tumor. There was a systolic murmur heard best at the pulmonic cartilage, and reduplication and accentuation of the second sound at this point. The other sounds were clear. The absolute liver dulness commenced at the sixth interspace. The lower border of the liver extended from the anterior superior spine of the ilium to the junction of the ribs and the anterior axillary line. It was firm, the surface smooth and not tender. It moved with respiration. The spleen was not distinctly palpable, but percussion indicated that it was enlarged. There was slight general anasarca, and œdema of the legs, extending to the knees. The knee-jerks could not be elicited, but otherwise the nervous system was negative.

The subsequent course of this case was quite uniform. The temperature was very irregular; there was nose-bleed almost daily, and this was usually severe and difficult to control. Emaciation progressed steadily, but very gradually. The liver gradually decreased in size. On June 10th it was one inch below the umbilicus, and on the 20th was barely below. The spleen remained enlarged by auscultatory percussion, and the lower edge was distinctly palpable. By July 1st the œdema of the legs had become quite severe; on the 14th there was a distinct accumulation of fluid in the peritoneal cavity, and on the 16th pronounced general anasarca. This persisted until death. The stomach was not enlarged. On July 19th he became slightly delirious, and had a convulsion, commencing in the hands and arms. After this he remained unconscious for some time. The muscles were spastic, but there was no paralysis. The pupils were equal and contracted. On the 20th of the month he was partially conscious and able to take nourishment, although still very restless. On the 21st there was slight tremor of the hands and some doubtful paresis of the left side of the face. When spoken to he answered only in monosyllables. Toward midnight he lapsed into complete unconsciousness, the pulse grew weaker, and he died at 2 A.M. July 22d.

Throughout the case the urine was examined, at first almost daily, and afterward at frequent intervals. On June 25th the specific gravity was 1020; albumin, sugar, and indican were absent. The diazo reaction was negative. The sediment contained a few leucocytes, but no casts. Subsequently there was occasionally a faint trace of albumin, constant toward the end; granular casts at rare intervals, and faint traces of bile twice. On the 28th the urea was found to be 228 grains in twenty-four hours (0.9 per cent.).

On May 24th the blood count was as follows: Hæmoglobin, 50 per cent.; red blood cells, 2,300,000; white blood cells, 4080. The leucocytes were counted at frequent intervals, and ranged between 3060 and 4380, with the exception of June 23d, when they reached 11,400 for some unexplained reason. The hæmoglobin decreased at first slowly; on the 20th the count



was 45 per cent., and 3,500,000. Later the anemia was more severe, and on July 8th the count was 20 per cent., and 2,800,000. The differential count on June 28th was: Polymorphonuclear cells, 81 per cent.; large mononuclear cells, 9 per cent.; small mononuclear cells, 10 per cent.; eosinophile cells absent. On June 25th a careful search failed to show the plasmodium of malaria. On May 30th the Widal reaction was reported positive, and on June 3d negative. On May 29th Justi's test for syphilis was negative. As it is of little value in the tertiary stage, this was not considered significant. The sputum contained staphylococci and streptococci, but never any tubercle bacilli. The stomach contents showed diminished solidity (18 per cent.); lactic acid was not present.

On June 1st the cyst was aspirated and a thick yellow fluid withdrawn, containing some cheesy masses. It also contained numerous compound granular cells, but no bacteria. The chemical examination gave reaction alkaline; specific gravity, 1030; albumin, 7 per cent.; albumoses present, evidently an inflammatory exudate. Tubercle bacilli in particular were not found. Cultures on various media remained sterile. Two guinea-pigs were subcutaneously injected, one of them dying ten weeks later of generalized tuberculosis, the other remaining healthy. June 20th 5 mgs. of tuberculin were injected. The temperature was lower than usual during the following twenty-four hours. On the 29th Prof. Edward Martin incised the cyst, and found it to consist of a cavity filled with cheesy masses, surrounded by a dense fibrous wall. It communicated by a narrow opening with a sub-sternal sinus that was apparently closed. Smears, cultures, and inoculations with this fluid, made by Dr. Kneass, were all negative.

The diagnosis of this case offered many difficulties. It presented the syndrome of progressive anæmia, with enlargement of the spleen and liver, associated with fever of extremely irregular type. After typhoid fever and malaria had been excluded, and the negative Justi test and failure to react to the antisppecific treatment had rendered the diagnosis of syphilis improbable, it appeared that the case must either be one of pseudoleukæmia, with irregular temperature, or a case of lymphatic tuberculosis—that is, Sternberg's disease. The latter supposition was slightly strengthened by the presence of a sign of mediastinal tumor, which consisted of the development of a harsh murmur over the base of the heart when the patient arched his back. This murmur, distinct from the hæmic murmur, constantly heard, was easily elicited. In view of the frequency with which cases of pseudoleukæmia prove to be tuberculous, and particularly on account of the irregular temperature, and the presternal abscess (a symptom of lymphatic tuberculosis first described by Askanazy), a positive diagnosis of lymphatic tuberculosis was finally made before Prof. Martin's operation. The autopsy was obtained with great difficulty, and not until forty-four hours after death. It was performed by Dr. Hendrickson, to whose kindness I am indebted for the following notes:

Intense edema throughout the body. Post-mortem decomposition well advanced. The abdominal cavity contained 800 c.cm. of blood-stained fluid. The liver extended 10 cm. below the costal border in the median line. The pericardial cavity was obliterated by firm adhesions. The weight of the heart was 420 grms. The walls were moderately hypertrophied, but post-mortem degeneration was so far advanced that it was impossible to determine anything further. The glands about the base of the heart were enlarged and caseous. The pleural cavities were obliterated by firm adhesions. The lungs contained numerous recent white miliary tubercles. The bronchial glands were enlarged and pigmented, but not caseous. The spleen was enlarged; it weighed 270 grms. It had undergone considerable post-mortem change, but numerous yellow conglomerate tubercles could be distinguished. The kidneys contained no tubercles. Both lateral lobes of the prostate contained caseous areas, that on the right side being greater. The liver weighed 2720 grms. Its surface was smooth; the lobules well defined, suggesting cirrhosis, and a few bile-stained conglomerate tubercles were scattered throughout its substance. The gastrohepatic and retroperitoneal lymph glands were greatly enlarged and caseous, but not all to the same extent. The aorta was slightly sclerotic. The brain, stomach, intestines, and pancreas were normal.

In view of these findings Dr. Hendrickson made the following diagnosis: General tuberculous adenitis. Chronic tuberculosis of the prostate (probably the initial lesion). Subacute disseminated tuberculosis of the liver and spleen. Acute disseminated tuberculosis of the lungs. Chronic obliterative pleuritis and pericarditis. Chronic subcutaneous tubercular abscess. He has also informed me that the histological examination of the tissues has confirmed in all respects the macroscopical diagnosis.

CASE III.—J. B., male, negro, laborer, aged thirty-six years, was admitted to my service at the Philadelphia Hospital, July 30, 1901. He was desperately sick and very unintelligent. He stated that his father and mother had died of asthma, and that three brothers had died in infancy of unknown causes. He had had most of the diseases of childhood and gonorrhoea; otherwise his health had been good.

His present sickness commenced at Christmas, 1900, when he was thrown from a wagon and fractured two ribs. From this time he had had pain in the chest and abdomen. During the month of June he commenced to cough and to expectorate a mucopurulent material that was never mixed with blood. He suffered from diarrhoea for several weeks; he lost considerable weight, and grew very weak; his appetite was poor and his sleep disturbed. For one week he had had only whisper speech.

When admitted it was noted that he was greatly emaciated; his expression was anxious; pulse rapid, weak, compressible, and regular. The tongue was slightly coated; the pupils reacted normally; there was complete aphonia; there were no pareses. The thorax was well formed; it

extended equally on both sides. The percussion note was impaired over the right apex, and over the left base posteriorly. Tactile fremitus and vocal resonance were slightly increased at the right apex. Fine crepitant râles were heard in both lungs anteriorly and posteriorly. The outline of cardiac dulness extended from the fourth rib downward, and from the left border of the sternum to the left parasternal line. The apex-beat was weak and circumscribed, and situated in the fifth interspace inside the nipple line. The sounds were clear, but very faint and distant. The liver dulness extended from the sixth rib to a line three inches below the costal margin, and to the left as far as the nipple line. The surface of the liver was smooth, and pressure upon it produced pain. The spleen was distinctly palpable as a large rounded mass in the left hypochondrium.

*July 31.* The urine contained albumin and granular and hyaline casts. The specific gravity was 1025. The sputum contained numerous tubercle bacilli.

*August 2.* The blood examination gave: Hæmoglobin, 60 per cent.; red blood cells, 4,190,000; white blood cells, 13,900. A differential count was not made.

*8th.* The patient had grown gradually weaker, and died at 8 A.M.

In view of the physical signs a diagnosis was made of miliary tuberculosis of the lungs, tuberculosis of the liver and spleen, general tuberculous involvement of the lymphatic system, and myocarditis. It was strongly suspected that the lymphatic involvement was primary on account of the marked enlargement of the liver and spleen. The autopsy was performed by Prof. Joseph McFarland, who had kindly permitted me to use his notes.

Autopsy performed eight hours after death. The pathological diagnosis was: General tuberculosis, most pronounced in the lymphatic apparatus and spleen; miliary tuberculosis of all organs; tuberculous ulcers of the stomach and intestines; acute hemorrhagic myocarditis.

The pleural and pericardial cavities were obliterated by adhesions and everywhere studded with yellow tubercles. Firm tumors, the size of lima beans, were found on the inner surface of the pleuræ. The base of the heart was surrounded by a large mass of tuberculous lymphatic glands. At the root of the aorta there was a single gland about the size of a hen's egg, firm in consistency, and resembling a fibroma upon section. It was encapsulated, and after section the cut surface became convex. The smaller glands were filled with yellow tubercles; both lungs were filled with gray tubercles. The heart weighed 620 grms. The epicardium was greatly thickened and gelatinous. The muscle was soft, yellowish in color, and everywhere studded with petechial hemorrhages. The spleen was enlarged, measuring 16 x 11 x 7 cm., and weighing 590 grms. It was firmly attached to all the surrounding surfaces by adhesions that included several cheesy lymphatic glands and a number of dark-colored hæmo-lymph glands. The substance was dark red in color, firm, and thickly studded with gray tuber-

culous areas, varying in size from a buckshot to a pigeon's egg. These were firm in consistency. The kidneys showed some parenchymatous degeneration and a few tubercles. The bladder and prostate were normal. The peritoneum was everywhere studded with miliary tubercles. The mesenteric glands were enlarged and tuberculous; about the coeliac axis they were as large as pigeon's eggs, and for the most part dense and hard. The liver was firmly attached to the diaphragm; it was enlarged, weighing 1690 grams. The section was nutmeg, and showed everywhere numerous miliary tubercles and a few bile cysts containing inspissated bile. The gall-bladder was thickened and small as the result of a chronic pericholecystitis. The pancreas was normal; the stomach showed numerous hemorrhagic erosions and a large ulcer near the pylorus. A few tuberculous ulcers were found in the intestines. There was a slight tuberculous erosion of the seventh rib on the left side and of the bodies of several vertebrae. The larynx was tuberculous.

Regarding the histological examination, Dr. McFarland writes me as follows:

The disease of the organs and lymphatic apparatus was tuberculosis. The large fibrous lymph nodes of the mediastinum, when examined microscopically, showed a chronic fibrosis, with scattered foci of cellular infiltration and coagulation necrosis. There were no typical tubercles present. The lymphatic tissue itself had disappeared. Except for the associated condition it would have been very difficult to recognize the true nature of the lesion.

CASE IV.—J. K., white, aged forty-nine years, stevedore, was admitted to the Philadelphia Hospital on July 29th, complaining of pain in the stomach, fever, and loss of appetite. His family history was too indefinite to be of value; his own previous medical history was also very unsatisfactory. He admitted gonorrhoeal infection thirty years ago; had been a moderate drinker, and three years ago had fractured his collar-bone. The ends of the bone had been wired together, but union had not occurred, and the sternal end of the outer fragment had penetrated the skin. His present disease began, according to his own account, about six months ago with an attack of jaundice. He was admitted to St. Mary's Hospital and treated for some time, and apparently recovered. After leaving the hospital, however, he had chills and fever, and from time to time severe hemorrhage from the mouth and nose. He rapidly grew weaker, his appetite was impaired, and he lost forty-two pounds in weight. When admitted to Dr. Stengel's ward at the Philadelphia Hospital his physical condition was as follows: A poorly-nourished, well-formed man, with a subicteroid tint of the skin; the pupils were normal; the tongue a good color, coated and slightly fissured. There was a large scar below the right clavicle at the sternal end, and at its

upper end a small necrotic mass of bone penetrated the skin. In the end of the bone several wire sutures could be seen. The skin around it was slightly discolored. There was slight pulsation of the veins at the base of the neck; the cervical glands were not enlarged; the pulse was of moderate force, quick, and receding; the vessels were soft; there was a distinct capillary pulse. The thorax was well formed; the expiratory movements were greater on the right side; respiration was vesicular; expiration was prolonged. On the left side inspiration was slightly diminished in intensity, and there was friction in the left axillary region. The apex was in the sixth interspace one inch outside the nipple line. The deep area of cardiac dullness extended from the right parasternal line to the left anterior axillary region horizontally and from the third rib above. At the apex the first sound was loud and sharp; the second sound was of moderate intensity. At the base both sounds were clear. The aortic second was louder than the pulmonic second. The liver extended from the sixth rib to a line one inch above the level of the umbilicus; the left lobe could be felt extending as far as the left nipple line; the surface was smooth and the liver was slightly tender. The spleen was not palpable, but appeared enlarged to auscultatory percussion. In the right lumbar region a smooth, regular mass could be felt, which seemed to be the right kidney. There was considerable gurgling in the abdomen upon deep palpation. The chest and abdomen showed some whitish areas. On August 1st a blood count was made and showed 4,530,000 red blood cells and 11,300 white blood cells. On the 12th the physical signs were as follows: On the right side inspiration was harsh; expiration was harsh and prolonged. On the left side inspiration was accompanied by creaking friction; expiration was soft and prolonged. The cardiac dullness extended horizontally from the mid-sternal to the left nipple line and from the third rib downward. The apex was in the fifth interspace one inch to the left of the nipple line. The heart sounds were clear; the pulmonic second was slightly accentuated. The liver extended from the sixth rib to the left of the umbilicus; it moved slightly with respiration, and was still distinctly tender. The spleen was not palpable, but was enlarged to auscultatory percussion. The abdomen was not distended.

Throughout the course of the case the patient had an extremely irregular temperature, but as the result of rest and feeding he improved slightly in his general condition. On the 21st he requested and was given his discharge.

In view of the irregular temperature, the enlargement and tenderness of the liver, the rapid loss of weight, the history of the hemorrhage, and the fact that nutrition must have been impaired as much as three years ago, all indicating a slowly progressive and very chronic condition, a diagnosis was made of lymphatic tuberculosis, although I felt at the time that there was a possibility that this was not correct.

On September 15th the patient was readmitted to the hospital, to the service of Dr. Riesman, suffering from cough and expectoration. The latter was examined, and tubercle bacilli were readily found.

On September 23d the patient stated that about the middle of the month he had had a severe hemorrhage from the nose, which had been repeated several times since then. His present condition is as follows: He is poorly nourished. There is marked pigmentation of the chest and back, with irregular areas of leucoderma. The right lung shows slight impairment of resonance at the apex; respiration is harsh and vesicular; expiration is prolonged. In the left lung resonance is impaired at the apex; respiration is faint and vesicular; expiration is prolonged; moist râles are heard at the apex during inspiration. The heart is enlarged; the apex is in the sixth interspace one inch outside the nipple line; it is feeble and diffuse. Dulness commences above, at the fourth rib, and extends laterally from the left border of the sternum to one inch to the left of the nipple line. The heart sounds are clear; the pulmonic and aortic second sounds are clear. The liver dulness commences at the sixth rib, and there is slight respiratory movement. The lower border can be palpated at the level of the umbilicus, and the lower lobe as far as the left nipple line. There is considerable tenderness over the liver. The spleen can be palpated during deep inspiration. By auscultatory percussion it appears to be considerably enlarged. The axillary and inguinal lymph glands are palpable but small. The cervical lymph glands cannot be felt. The pulse is medium, full, of normal volume; the arteries are soft; the knee-jerks are normal, and there is no disturbance of sensation. The patient has cough and expectoration, and tubercle bacilli are readily found in the sputum.

The patient continued to grow worse. The physical examination showed very little change, excepting that the skin grew noticeably darker over the whole body. On November 9th the presence of a considerable quantity of fluid in the abdominal cavity was recognized. The liver and spleen were both palpable, and the patient was very weak. On November 17th he died. The only examination of the urine made during his last stay at the hospital showed a specific gravity of 1010; no albumin and no sugar. The autopsy was made by Dr. Buckley on the day of death. The pathological diagnosis was miliary tuberculosis of both lungs; pleurisy, with effusion on the left side; tuberculous ulcers of the intestines; cirrhosis and fatty infiltration of the liver; parenchymatous nephritis, and a tapeworm. The weight of the spleen was 250 grms. and of the liver 1570 grms. There was fluid in the left pleural cavity; the spleen contained numerous tubercles; the glands of the mesentery and mediastinum were only slightly enlarged. Otherwise nothing of importance was found.

Dr. M. P. Ravenel very kindly consented to make cultures from the glands, which were not as greatly enlarged as I had expected to find them. No tubercle bacilli were found upon staining, but guinea-pigs inoculated



with the granular substance died with generalized tuberculosis, and Dr. Ravenel states that there is some reason to believe that this bacillus is more virulent than the variety ordinarily obtained from human beings. The cultures have not yet been completed.

*Summaries of the Four Cases.*

I. The disease commenced with cough and expectoration, followed by weakness and loss of weight; then pain in the back, chills and thirst. Four months later the liver and spleen were found to be enlarged, and there were signs of catarrhal disease at the right apex, and a slight anæmia. The urine contained albumin and blood casts. In the course of a few weeks tubercle bacilli were found in the sputum, ascites developed and the patient died of pulmonary œdema. At the necropsy there was found miliary tuberculosis of the lungs and liver, and there were tuberculous ulcers in the intestines.

II. A man, aged twenty-eight years, as a result of a severe strain, developed a fluctuating tumor over the sternum. Shortly after this he noticed enlargement of the liver. Two years later he had pain in the back, cough and expectoration, profuse epistaxis and fever. When admitted an abscess containing sterile pus covered the lower part of the sternum. The liver and spleen were enlarged; the resonance at the right apex was slightly impaired: a hæmic murmur was heard at the base of the heart; the temperature was irregular; the blood showed moderate anæmia and the urine a slight amount of albumin. He finally developed general œdema and ascites, had a slight apoplectiform attack, and died. At the necropsy there were found an adherent pericardium, caseous and fibrous mediastinal and abdominal lymph glands, recent miliary tuberculosis of the lungs, conglomerate tubercles of the spleen and liver, and old tuberculosis of the prostate gland.

III. Six months after an injury to the chest the patient developed cough and expectoration. He had diarrhœa, was emaciated, and slept poorly. When admitted he had aphonia, impaired resonance at the right apex, a feeble heart-beat, enlargement of the liver and spleen, albuminuria, and moderate anæmia. The sputum contained tubercle bacilli. At the necropsy there was found general tuberculosis, most pronounced in the lymph glands and spleen: miliary tuberculosis



of all the organs, tuberculous ulcers in the intestines, obliterative pericarditis and pleuritis and hemorrhagic myocarditis.

IV. A man, aged forty-six years, fractured his clavicle, and in spite of wiring union did not occur. Two and a half years later he had an attack of jaundice, then chills and fever, and hemorrhages from the mouth and nose. The liver became enlarged and tender; the spleen was moderately enlarged; there was moderate anæmia without leucocytosis. The temperature was irregular. From time to time he had hemorrhages from the nose; the liver and spleen increased in size; the superficial glands were palpable, but small. He developed the physical signs of pulmonary tuberculosis, and tubercle bacilli were found in the sputum. Finally, there was a severe ascites and death. At the autopsy the abdominal and thoracic lymph glands were found moderately enlarged. There was a subacute miliary tuberculosis of the spleen, fatty degeneration, but no tuberculosis of the liver. There was miliary tuberculosis of the lungs and tuberculous ulcers in the intestines. Dr. Ravenel made cultures from the lymph glands and found an actively virulent tubercle bacillus.

These four cases have so many clinical and pathological features in common that they may properly be considered as belonging to the same group. In all there was moderate anæmia, progressive cachexia, terminating in death, and enlargement of the liver and spleen. In the case longest under observation (II.) the temperature was unusually irregular. In the other three cases it was not taken continuously, but was quite irregular for periods of several days. Case III. was under observation a very brief time. In two cases (I. and II.) there was almost constant œdema, and in three (I., II. and IV.) a terminal ascites. In three cases (I., III. and IV.) the liver was exquisitely tender, and in the other it had been enlarged for two years, and was almost painless. In three cases (I., III. and IV.) tubercle bacilli were found in the sputum before death, and in the other a lesion, probably but not certainly tubercular, existed. The post-mortem findings in three cases were very similar. There was enlargement of the deep lymphatic glands, miliary tuberculosis of the lungs, subacute tuberculous of the liver and spleen, and in one case tuberculous erosions of the bones. The subcutaneous

densely encapsulated sterile abscess in Case II. was similar to the fluctuating tumors situated close to the spinal column observed by Askanazy in a woman of thirty-seven who was suffering from anemia. These contained a sterile, partly cheesy material that could only be withdrawn through an incision, and each communicated with the thoracic cavity by a narrow sinus. Case III. had a huge fibrous encapsulated tumor at the base of the heart that resembled very closely the tumor described by Claessen, occurring in a boy aged nineteen years who had chronic passive congestion of all the organs, enlargement of the liver and spleen, and symptoms of chronic obliterative pericarditis. This tumor resembled a fibroma and showed no areas of necrosis, but tubercle bacilli were found in its substance. The bronchial glands were caseous, and miliary tubercles were found in the pleuræ and pericardium, but the lungs and other organs were free. Probably similar tumors are described by Wunderlich and Langhaus. It was found at the autopsy of a case suffering from chronic recurrent fever, but tubercle bacilli were not demonstrated in it. In Case IV. the findings were rather atypical inasmuch as the deep lymph glands were not greatly enlarged. There was, however, a subacute tuberculosis of the spleen and miliary tuberculosis of the lungs, and in addition, tuberculous ulceration of the intestines. Fortunately the inoculation experiments by Dr. Ravenel prove conclusively the tuberculous nature of the process in the lymph glands.

It may be said to be the prevailing opinion among pathologists of the present day that there are three forms of disease of the lymph glands that may give rise to the syndrome that is said to be characteristic of pseudoleukæmia. These are lymphosarcomatosis, tuberculosis, and a peculiar infectious process whose cause has not yet been discovered, but which by some (Reed) is regarded as the only true form of Hodgkin's disease. The relation of the tubercle bacillus to Hodgkin's disease has been a subject of interest for many years. Billroth long ago suggested that the hard fibrous form of lymphadenitis was really a tuberculous infection of the lymph glands. In 1875 Winiwarter wrote that "some have endeavored to find in syphilis and tuberculosis an etiological factor for malignant lymphoma: at present there is nothing to prove this." Of late years a considera-

ble amount of proof has been furnished, although the opinions of the authorities are much at variance. With the possible exception of Sternberg, I have been able to find no authority who declares himself unqualifiedly in favor of the theory that pseudoleukæmia is always produced by infection of the lymphatic apparatus with tubercle bacilli. But even Sternberg is not dogmatic, although he regards this view with considerable favor. That the glands in many instances contain tubercle bacilli is no longer a matter of question, and that these bacilli are capable of infecting susceptible animals has been conclusively proven. Moreover, it has been shown that in many cases the characteristic histological picture of lymph gland tuberculosis does not exist, although the tubercle bacilli may be numerous and virulent. It does not necessarily follow, however, that they are the cause of the pseudoleukæmia, because, as many authors have suggested, they may exist either as a secondary or as an associated infection. That is to say, there is no reason why lymph glands, the seat of tuberculosis, might not take on the changes and produce the symptoms of pseudoleukæmia, or that lymph glands characterized by the morbid alterations of pseudoleukæmia and associated with symptoms of that disease, might not become infected with tubercle bacilli. The latter view is held by Liebmann, Dietrich, Schmalz, Koster, Fischer and others. Some of these authorities also believe that tuberculous infection of the lymph glands may under certain circumstances produce morbid changes somewhat similar to those of pseudoleukæmia, and that the symptoms of the disease may be indistinguishable. Stengel, Fröhlich, Liebmann, Dietrich, Finzi, Combemale and others who have written within the last decade admit the tuberculous nature of some cases of pseudoleukæmia. However, they insist that it can also be produced by other hitherto undiscovered causes. Weiss and Reed, I believe, are the only authors who assert that, although lymph glands may be infected with the tubercle bacilli and may give rise to the symptoms of pseudoleukæmia, nevertheless, all such cases should be considered as merely instances of lymphatic tuberculosis not belonging to the pseudoleukæmic group. In fact, they believe that they differ essentially from this group in their morbid anatomy and in their etiology. Pinkus, one of the most recent writers on the subject, after a brief

summary of the facts at hand, states, very fairly I think, that "the question whether tuberculosis is invariably present in those glands which show signs of pseudoleukæmia can only be decided by a considerable increase of the available material. The fact that the more carefully the investigations have been conducted with all the aids of modern knowledge, the more frequently has the tuberculous nature of the process been proven, argues strongly for the influence of tuberculosis in these cases."

When we sift the mass of clinical and pathological material that has been accumulated in the literature, we find that the greater proportion of it furnishes merely presumptive and not conclusive evidence. In the majority of cases that have been reported no effort has been made to find tubercle bacilli unless certain characteristic lesions were present. On the other hand, in many instances what were apparently miliary tubercles have been regarded as the metastases of lymphosarcoma, and described as such without the exclusion of tuberculosis by histological examinations, cultures, or inoculations. It must be stated, however, that a considerable number of these cases were observed before the discovery of the tubercle bacillus, and, therefore, before it was possible to identify the nature of the lesions. Among these are the cases reported by Winiwarter, Langhans, Kuhnherm, Desmos and Barić, Arkmann, Wendt, Rosenstein, Perret, Morrison, Pantoppidan, and Schmidt. In other cases, although the prevailing views of the nature of the process and the belief that the cause was unknown led to the neglect of careful investigations, the reason to suspect the existence of tuberculosis was very strong. For example, there has been cheesy degeneration in the glands, as in the cases of Brauneck and Winiwarter; amyloid disease of the organs, as in the cases of Buchanan and Pantoppidan; necrosis and softening of the glands, as in the cases of Winiwarter and Mosler. Other cases have been recorded in which the clinical course resembled in many respects that which, we believe, is typical of lymphatic tuberculosis, but in which the autopsy is either lacking or so inadequately reported that it is impossible to draw any conclusions from it. Among these are the cases of Mosler, Liebmann, Turk, Sippi, and Russell.

The cases that have been sufficiently well studied to furnish direct

evidence upon this question are few in number. They include those in which tuberculosis of the lymph glands and possibly of other organs existed and was positively demonstrated by inoculations or by staining the tubercle bacilli. Second, those in which careful histological and bacteriological examinations excluded the existence of the tubercle bacillus.

Among the earliest cases of the first group was that of Delafield. His patient, a woman twenty-three years of age, had enlargement of the cervical lymph glands, an irregular and often high fever, progressive emaciation, and death. At the necropsy there was found calcification of the mesenteric glands, evidently a chronic process, and miliary tuberculosis of the lungs. The next case, reported by Waetzold, was of the utmost importance, because it was the first in which tubercle bacilli were demonstrated in glands which failed to show the characteristic histological changes, and, therefore, called attention to a form of tuberculous infection hitherto unrecognized. A woman thirty years of age had had glandular swellings in childhood; these reappeared three and a half years before death, and were extirpated. Immediately afterward the patient developed anorexia, diarrhoea, cough, and progressive weakness. One and a half years before death the glands were again extirpated, and histologically appeared to be pure lymphomata. After this the emaciation became extreme: there was complete insomnia; the cough was worse and not controlled by drugs, although there were no signs of pulmonary disease. The temperature showed irregular elevations, and there were chills and epileptoid attacks that apparently improved upon quinine. Dry pleurisy, ascites, and albuminuria developed, and the inferior maxillary glands underwent softening just before death. The necropsy revealed enlargement of the spleen: the retroperitoneal and mesenteric glands were enlarged; there were amyloid kidneys, a normal liver, and miliary tuberculosis of the lungs. The mediastinal and bronchial lymph glands were also enlarged and contained hyaline areas in which there were numerous tubercle bacilli.

A still more remarkable case was reported the following year by Brentano and Tangl. A woman fifty-seven years of age had swelling of the inguinal and cervical glands, irregular fever, with evening

rise, ascites, pleural exudate, progressive anemia and cachexia, and death. The necropsy showed enlargement of the mediastinal, mesenteric, and retroperitoneal lymph glands, chronic peritonitis, tuberculosis, and ulceration of the intestines. The liver was not enlarged. The lymph glands were not necrotic, and presented none of the histological characteristics of tuberculosis, but inoculation of a guinea-pig with the glandular substance caused death from tuberculosis. The authors contended that this case proved that negative histological evidence is insufficient to exclude tuberculosis, although it must be admitted that a single inoculation experiment is not absolutely conclusive.

In 1893 Cordua described some glands removed from a woman twenty-two years of age who was supposed to be suffering from Hodgkin's disease. The clinical history is incomplete. The glands, upon histological examination, presented the appearance ascribed to Hodgkin's disease, but Cordua was able to demonstrate the presence of tubercle bacilli in their substance. He calls the disease malignant leukæmic lymphoma, apparently not regarding the presence of tubercle bacilli as excluding Hodgkin's disease. A similar case was reported by Sabrazès in 1891, who, however, only proved the tubercular infection of the glands by inoculation.

In 1894 and later Askanazy reported three cases. The first, a woman thirty-two years of age, had enlarged glands in the neck, an enlarged liver, and recurrent fever. At the necropsy the mediastinal and bronchial lymph glands were enlarged, but the spleen and retroperitoneal glands were normal. Tubercle bacilli were found in the lymph glands. The second case, a woman thirty-seven years of age, complained of pain in the left side of the chest. There was severe anæmia and fluctuating tumors arising from the ribs on the left side. These were incised and found to contain a sterile, cheesy material, and to communicate with the thoracic cavity through narrow sinuses. Tubercle bacilli were not found in the sputum. At the necropsy the mediastinal glands were found to be enlarged and partly necrosed, and showed marked tendency to fibroid induration. The liver was enlarged and contained numerous tubercles. The retroperitoneal lymph glands were greatly enlarged, and guinea-pigs inoculated with the glandular tissue developed

tuberculosis. Microscopically, the glands exhibited the characteristic picture of tuberculosis. The third case, a woman thirty years of age, complained of chills, night sweats, and expectoration. There was moderate anemia and fever of an irregular type. She developed hydrothorax, and later a hard, immovable tumor appeared in the neck. Tubercle bacilli were found in the sputum. At the necropsy all the glands were found to be enlarged and firm, but not necrotic. The liver was enlarged and contained yellow nodules. The costal pleura was greatly thickened and dense. All the organs presented the characteristic histological changes of tuberculosis, and tubercle bacilli were found in the tissues. Askanazy calls attention to the many features of resemblance between this case and pearl disease in cattle, a valuable suggestion, which I shall discuss more thoroughly later.

In 1898 Sternberg published a paper that he had evidently had in preparation for a considerable time. In view of the occasional discovery of tubercle bacilli, or the evidence of tuberculous infection in a number of cases that clinically resembled pseudoleukemia, he determined to study the tissues from a considerable number of cases, in order to determine whether the micro-organism bore any actual relation to the disease or not. For this purpose he obtained specimens from eighteen cases of pseudoleukemia, of which he says fifteen, in their anatomical changes and usually in their clinical course, resembled the peculiar cases of pseudoleukemia which had attracted his attention. For reasons that Sternberg does not explain, the clinical histories of his fifteen cases are not given; in fact, in some even the clinical diagnosis is lacking, and it is not, even when given, always pseudoleukemia. But it is not improbable that in all cases pseudoleukemia was suspected at some time in the course of the disease.

Briefly epitomized the cases are as follows: Case I. Clinical diagnosis: Pseudoleukemia, bilateral pleuritis sicca, miliary tuberculosis (which was doubtful), and splenic tumor. The lymph glands were generally enlarged and formed tumor-like masses in the mediastinum and retroperitoneal space. The spleen was enlarged and contained numerous white nodules. The right pleural cavity was obliterated by adhesions, and the left contained clear fluid. The right



lung was filled with grayish nodules. There was clear fluid in the abdominal cavity. The nodules sometimes showed necrosis, and in some of them a few tubercle bacilli could be demonstrated.

Case II. Clinical diagnosis: Pseudoleukæmia. The lymph glands were enlarged, and several had suppurated or showed caseous degeneration. The liver and spleen were enlarged and showed numerous tubercles; the bone marrow was embryonal. The histological picture was in general that of tuberculosis, but tubercle bacilli could not be found.

Case III. No clinical diagnosis. The lymph glands were enlarged and in part caseous. The spleen was enormously enlarged and contained numerous miliary tubercles. There was general icterus. The tissues contained necrotic areas with giant cells, but tubercle bacilli were not found. There was general arterio-sclerosis.

Case IV. Clinical diagnosis: Pulmonary tuberculosis, cirrhosis of the liver (considered doubtful), and degeneration of the myocardium. There was enlargement of the lymph glands and of the liver and spleen, and the latter contained miliary tubercles. The histological changes were those of atypical tuberculosis; tubercle bacilli were not found.

Case V. No clinical diagnosis. The lymph glands were enlarged; the spleen and liver were enlarged and contained numerous tubercles. The tissues showed atypical tuberculous lesions, and these contained numerous tubercle bacilli. The tissues from Cases II., III., IV., and V. had been preserved for many years.

Case VI. Clinical diagnosis: Pseudoleukæmia, icterus, due to compression of the common duct by swollen lymphatic glands. The lymph glands were generally enlarged and necrotic; there was chronic tuberculosis of the right lung. The spleen was enlarged and contained numerous miliary tubercles; there were ulcers in the cæcum. The histological changes indicated tuberculosis, but tubercle bacilli were not found.

Case VII. Clinical diagnosis: Chronic tuberculosis of the lymph glands and serous membranes. There was universal œdema, profound anæmia, enlargement of the lymph glands and spleen, subacute nephritis and hypertrophy of the left ventricle. Cheesy areas, giant cells, and tubercle bacilli were not found in the tissues. The spleen showed considerable amyloid degeneration.

Case VIII. Clinical diagnosis: Pseudoleukæmia, with recurrent fever. There was tuberculous infiltration

of the apices of both lungs: the lymph glands were enlarged and firm: the liver and spleen were greatly enlarged, and contained white masses and miliary tubercles. The tubercles were composed of cellular aggregations and necrotic areas containing giant cells and a few tubercle bacilli. Case IX. Clinical diagnosis: Tuberculosis, pseudoleukæmia, tuberculous infiltration of the right lung, compression of the common duct by enlarged glands. There was enlargement of the lymph glands, with caseous degeneration. The liver and spleen were enlarged: the bone marrow contained numerous nodules, which showed cellular proliferation and some necrosis that was not caseous. Tubercle bacilli are not mentioned. Case X. A boy ten years of age, with typical pseudo-leukæmia. An extirpated gland showed cellular proliferation, with necrotic areas: tubercle bacilli were not found. Case XI. No clinical diagnosis. The anatomical diagnosis was pseudo-leukæmia and tuberculosis of the retroperitoneal lymph glands. The liver and spleen were enlarged and contained numerous nodules. The retroperitoneal glands were also greatly enlarged, and consisted of fibrous tissue containing spindle cells, lymphocytes, and giant cells. The borders of the glands were very red. Case XII. Clinical diagnosis: Tuberculous pseudoleukæmia, tuberculosis of the lung and lymphatic glands, and enteritis. Anatomical diagnosis: Lymphosarcoma of the lymphatic tissues and chronic tuberculosis of the glands. The lymph glands contained a large amount of fibrous tissue, groups of spindle and giant cells, proliferated endothelial cells, and erythrocytes. In some cases cheesy degeneration was present, and tubercle bacilli were found in the lymph glands. Case XIII. Clinical diagnosis: Pseudoleukæmia. Anatomical diagnosis: Pseudoleukæmia, with general enlargement of the lymph glands and spleen, hydrothorax, and ascites. The lymph glands and spleen showed fibrous alterations, enlargement of the capillaries, and desquamation of the epithelium. Case XIV. Clinical diagnosis: Tuberculous lymphadenitis; marked tuberculosis of the lungs: spleen greatly enlarged. The lymph glands were enlarged and contained necrotic areas and foci of epithelioid and giant cells. Tubercle bacilli could be demonstrated in the serous membranes. The liver contained numerous nodules. Case XV.

Clinical diagnosis: Pseudoleukæmia and tuberculosis of the lungs. Anatomical diagnosis: Miliary tuberculosis of the lungs, cirrhosis of the liver, tumor of the spleen, and marked tuberculosis of the lymph glands. The lymph glands showed caseous degeneration, and tubercle bacilli were found in them and in the spleen. The liver contained numerous nodules.

The critical examination of these cases is not entirely as favorable to the relation between tuberculosis and pseudoleukæmia as the enumeration appears to prove. In Delafield's case the clinical symptoms of pseudoleukæmia were not distinct enough to enable a diagnosis to be made. In Waetzold's case the long course of the disease renders secondary infection with tubercle bacilli possible, and the same may be said of the case reported by Brentano and Tangl. The cases of Cordua and Sabrazés appear to be more certain. The clinical course and the histological changes in the glands were identical with pseudoleukæmia. There were no evidences of tuberculosis in other parts of the body, or of tuberculous cachexia: nevertheless tubercle bacilli were demonstrated in the glands removed by operation. Askanazy's first case also appears to be very conclusive, but the second and third cases may merely have represented diffuse tuberculosis of the lymphatic glands and not pseudoleukæmia. The fifteen cases of Sternberg are not all of such character as to prove his contention regarding the relation of the two conditions. It will be noted that the clinical diagnosis of uncomplicated pseudoleukæmia was made only in three cases, and that of recurrent fever—that is, Ebstein-Pel's disease—in two others. In two cases the diagnosis was pseudoleukæmia complicated by tuberculosis, and in a third, tuberculous complication was considered probable. In four cases a diagnosis was made of lymphatic tuberculosis simulating pseudoleukæmia; and in one the diagnosis was pulmonary tuberculosis and cirrhosis of the liver, a condition which it appears difficult to differentiate from pseudoleukæmia due to tuberculous infection. In three cases no diagnosis is given. In these fifteen cases no inoculation experiments were made; no cultures were made, and tubercle bacilli were found in only five instances. Therefore, Sternberg's diagnosis of tuberculosis was made in the remaining cases because of the presence of lesions resembling those found in the tissues of the

cases in which tubercle bacilli were demonstrated, but not resembling the lesions ordinarily found in tuberculosis of the lymph glands, and therefore not certainly the result of the activity of the tubercle bacillus. If it were not for the cases that have been already reported we should be obliged to regard the work of Sternberg as doubtful. It is only the fact that this work confirms so thoroughly the results obtained by the others who have made careful examinations of the lymph glands in cases of pseudoleukaemia that we are justified in considering it as establishing his contention that in a large proportion of the cases supposed to be pseudoleukaemia the tubercle bacillus is present either as a causative or as an associated factor.

The negative evidence is even more scanty, and in view of the incomplete studies made in the majority of cases, far less satisfactory. In 1891 Czerny reported the case of a boy of four years who had a tumor on the right side of the neck. There was continuous fever, moderate leucocytosis, progressive anæmia, enlargement of the liver and spleen: pain in the abdomen, and emaciation. Shortly before death there was epistaxis and anasarca. At the autopsy a purulent exudate was found in the abdomen; the liver and spleen were enlarged and contained miliary nodules. The histological appearances were not characteristic of tuberculosis, and tubercle bacilli could not be found. Five years later Dietrich reported three cases with enlargement of the cervical and axillary glands. In one of these cases there was considerable fever, emaciation, and œdema: the spleen and liver were enlarged and contained necrotic areas in which giant cells were found. The lymph glands were enormously enlarged. In another case the cervical and axillary glands were enlarged and contained necrotic areas, but tubercle bacilli were not found. But as the tissues had been hardened in Müller's fluid, it is possible that they had lost their staining power. Inoculations were not made, and for that reason the evidence must be regarded as doubtful. In 1897 Fischer, stimulated by Dietrich's paper, attempted an experimental investigation of the whole subject. Unfortunately this was only published in the form of a lecture, and the details of the individual cases were not given. His general results though are stated clearly. In all he studied twelve cases, ten men and two women. In none of them was there leucocytosis,

and cultures and inoculations made from the blood were negative, with the exception of one case of recurrent fever in which the inoculations were positive during the febrile periods and negative during the intervals. He does not state the nature of the organism found, but merely calls it "secondary infection." Four of the cases died, and in all there was general involvement of the lymphatic structures in the lymphomatous change. One of these cases had, in addition, tuberculosis of the lungs and mesenteric glands, and another tuberculosis of the lungs, spleen, and liver. In both the process was recent, and must therefore be regarded as secondary infection. In all the cases the glands were extirpated, and from these glands inoculations, cultures, and histological examinations of the tissues were made. The guinea-pigs inoculated were killed two or three months later, and only one showed any tuberculous change, and this was not in either of the cases complicated by tuberculosis. Cultures and histological examinations were negative, and eosinophile cells were found in great numbers in the glandular substance. According to Kanter, who has made a careful study of the changes in lymphomatous and tuberculous lymph glands, and has reached the conclusion that they are essentially independent diseases, although they may coexist, eosinophile cells are strongly against the existence of tuberculosis. Fischer does not share this view. The positive case was a girl of sixteen who had enlarged cervical glands. They were removed, and found to contain numerous eosinophile cells, but no areas of necrosis and no giant cells. Tubercle bacilli could not be stained, but fragments of the glands inoculated into two rabbits caused their death in seven or eight weeks, and both presented typical tuberculous lesions. Later the patient developed tuberculosis of the lungs, and the tubercle bacilli could be demonstrated in the sputum, and the scar of the operation by which the glands had been removed reopened and suppurated. This case seems particularly valuable for the purpose of proving that in the absence of the characteristic histological changes of tuberculosis, or of the ability to stain the tubercle bacilli in the tissues, tuberculous infection may exist. Since Fischer's paper no important article has been written excepting that of Freudenweiler. He reports the case of a woman, aged thirty-one years, who at the age of thirty had swelling of the

cervical lymph glands, then pain in the abdomen, followed by swelling, and finally ascites. She became cachectic, and there was profuse diarrhoea. She then developed a large abscess in the wall of the abdomen, which ruptured spontaneously, the pus of which was sterile. Animals inoculated with this pus did not develop tuberculosis. At the autopsy the cervical and mesenteric lymph glands were enlarged, and the latter were cheesy. There were ulcers in the gastrointestinal tract, but there were no nodules in the spleen or liver. The glands showed no characteristic changes of sarcoma, and in the cervical glands there were added to these the changes characteristic of tuberculosis. The diagnosis, therefore, is one of lymphosarcoma, which he believes developed in the tuberculous glands.

In this series of cases the only ones of any value are those of Fischer, and even they appear to be insufficient to establish the conclusion that pseudoleukæmia is sometimes due to other lesions than tuberculosis. It is almost unnecessary to call attention to the valuelessness of the inability to discover the tubercle bacillus in the glandular tissues as a proof that tuberculosis does not exist, for in the cases of Sabrazès, Fischer, and Brentano and Tangl tubercle bacilli were not found, and yet the inoculations were positive, and the same thing was true of Case IV. in my series. Inoculations, too, can only be regarded as satisfactory evidence if they are made in sufficient number, or if the results are positive. In Case II. of my series the presternal abscess was unquestionably tuberculous, and yet only one of two guinea-pigs inoculated with a large quantity of the pus developed tuberculosis. Nevertheless, it must be admitted that Fischer's paper furnishes the strongest evidence, and practically the only absolute evidence that we have at present, against the tuberculous theory of Hodgkin's disease. Accepting it, therefore, we are obliged to consider three possibilities: either the etiology of Hodgkin's disease, so called, is multiple, that is to say, there are a variety of factors that can cause it; or that there is some other single etiological factor, and that the tubercle bacillus when it does occur in the gland must be regarded as an accidental or mixed infection, or that our present methods of detecting the presence of the tubercle bacillus are inadequate in some instances. There is no particular reason why the first of these possibilities should not be so, because in other

conditions with similar clinical course, such as cerebro-spinal meningitis, the variety of etiological factors is considerable. If the second supposition is correct we should expect to find tuberculous infection not so infrequently in cases of leukæmia, and also occasionally in other forms of tumor. It is of course well known that cases of pseudoleukæmia may present a terminal leucocytosis (Fleischer and Penzoldt) and present before death the characteristic picture of leukæmia. In 1892 Francksen, whose original paper I have been unable to procure, was able to collect a few cases in which leukæmia and tuberculosis apparently co-existed. In 1900 Junger reported an additional case in a man, twenty-five years of age, who had a sudden swelling of the tongue which was relieved by a copious discharge of pus, cedema of the hands and feet, enlargement of the cervical, axillary, and inguinal glands, and of the spleen. There was bronzing of the skin. The leucocytes were at first 40,000 and later 125,000. The fever was intermittent and the temperature often fell below 35°. The patient died, and at the autopsy miliary tubercles were found in all the serous membranes and in the liver and spleen. The hyperplastic lymph glands were also tuberculous. In the blood from the hemorrhagic lymph glands tubercle bacilli could readily be demonstrated. The lungs were free. He supposes that the case was one of latent tuberculosis awakened by the development of the leukæmic process. The following year Sturmldorf reported a case occurring in a woman thirty-five years of age, who at the age of thirty-three developed enlargement of the spleen. Two years later she awoke one morning with pain in the throat, cough, and hoarseness. She lost weight: there were moderate fever, tuberculosis of the larynx, and the characteristic blood picture of leukæmia, the leucocytes being 156,000. The fever was irregular, and it was found that the myelocytes varied inversely with it. Tubercle bacilli were readily demonstrated in the sputum. This case can easily have been a tuberculous infection of the larynx complicating leukæmia.

In regard to the infection of other forms of tumor with tuberculosis, the evidence derived from a study of the literature would seem to indicate that it is of the rarest occurrence. In 1895 Ricker reported two extraordinary cases. A woman was operated on for



sarcoma of the breast. Two years later there was recurrence, with the symptoms of general sarcomatosis, followed by death. The necropsy showed miliary tuberculosis of the lungs, which contained hard nodules without caseation or giant cells, and great enlargement of the spleen, which contained miliary tubercles. In the breast there were two tumors, one caseous, the other resembling the metastases in the lungs, but containing giant cells. Tubercle bacilli were found in both tumors. Ricker admits that this was possibly a secondary infection of the tumor from tuberculous lesions that already existed in other parts of the body. He argues against this, however, that there is no other case on record in which a tumor has become infected in this manner, or in which a wound has become infected during operation, nor is there any case on record in which a wound has become infected as a result of tuberculosis in other parts of the body, leaving the impression that it is his belief that either sarcoma and tuberculosis co-existed, or that the process was tuberculous from the beginning. The second patient was a boy who at the age of ten years had some swollen lymph glands removed from the neck. These recurred, and at the age of fifteen years the boy was brought to the hospital emaciated, pale, and complaining of severe pains in the lumbar region. A diagnosis of lymphosarcoma was made. Subsequently paraplegia developed, and the patient died. At the necropsy large tumors were found in the neck, in the mediastinum, in the lungs, and in the bodies of the vertebrae. These tumors showed the structures of lymph glands. Scattered throughout the lymphoid tissue there were groups of six or seven endothelial cells, but typical giant cells were absent. Great numbers of tubercle bacilli were found in the sections. Ricker regards the tubercle bacilli as undoubtedly the cause of the tumors in this case, although he admits that further investigations are necessary in order to determine what relation the tubercle bacillus bears to malignant lymphoma or lymphosarcoma. He is convinced that when it involves the lymphatic tissues it can produce a clinical type of disease that differs greatly from the ordinary pulmonary form. In 1899 Warthin reported two cases of carcinoma of the breast—the first appeared, three years after the organ had ceased to functionate, as a small lump that grew rapidly, in a woman of forty-two years. At the same

time there was enlargement of the glands in the axilla. The breast softened and an abscess was found in it, and after a partial amputation the patient made a perfect recovery. Histologically it showed the characteristic picture of carcinoma simplex associated with tuberculosis, and tubercle bacilli were found in the pus. The other, a woman of thirty-nine years, had carcinoma of the breast with metastases to the axilla. Carcinoma associated with tuberculosis was found both in the breast tissue and in the involved glands. But on account of the hardening fluid (Müller's) tubercle bacilli could not be stained. He accepts Lubarsch's classification of these structures.

I am inclined to believe that these cases are analogous to the cases which have been reported of lupus and carcinoma of the skin, and tuberculosis and carcinoma of the oesophagus and larynx. Of the latter a number of cases are now on record, particularly those of Cordua, Michaux, Setulle, Zenker, Pepper and Edsall. These cases are characterized usually by the presence of old tubercular lesions in the lungs and the absence of metastases to the glands surrounding the structures, although Michaux states that in his case some of the glands were softened and some firm and white as in glands affected by carcinomatous metastases. As no histological examination was made his statement must be received with reservation.

I think there is considerable doubt regarding the nature of these so-called carcinomatous tumors. Ribbert has shown that epithelium separated from its basement membrane by pathological processes may proliferate, and he attempts to find in this an explanation for the cause of carcinoma. It is possible that in these circumstances, however, the proliferation, although morphologically similar, is etiologically distinct from that characteristic of the true carcinomatous growth. The long history of some of these cases seems to be strongly against a malignant proliferative process.

The evidence regarding the tuberculous nature of pseudoleukæmia, aside from that which we have quoted, is so scanty and inconclusive as to be almost worthless. Delbet inoculated a dog with bacilli whose nature is not mentioned from a case of lymphadenoma and produced chronic abscesses with enlargement of the lymph glands. Galasso has observed improvement in cases of tuberculous lymphoma after the use of Maragliano's serum. Jaccoud, Mosler and Birch-

Hirschfeld have observed infectious adenitis following infectious diseases. Tuberculosis, of course, often follows infectious disease, but there is no other reason for supposing the two processes the same. Liebmann has observed miliary tuberculosis as a complication of adenitis. He supposes that it may be a true complication, or else either assume the appearance of adenitis or actually cause it. Philipart calls attention to the similarity between a case of cutaneous lymphomata and leprosy.

Assuming the tuberculous nature of these conditions, the question naturally arises why tuberculosis of the lymph glands sometimes produces such extraordinary symptoms. In 1894 Askanazy suggested that the lesions in one of his cases resembled pearl disease in cattle. In 1898 the careful studies of Theobald Smith proved that there was more than one variety of the tubercle bacillus. He believed at that time that the chief distinction lay between the bovine and human tubercle bacillus, and that the greatest difference existed in the degree of virulence of these two organisms. His paper has since been amply confirmed by Koch, Ravenel and others; Koch even going so far as to claim that human tubercle bacilli were not pathogenic for cattle, nor the bovine tubercle bacilli for human beings, a statement that has been conclusively disproved by the work of Ravenel. In 1901 Lartigau showed that a considerable variation existed between specimens of tubercle bacilli obtained from different lesions in human beings, and Ravenel has found the same thing to be true. It seems possible, therefore, that perhaps in the pseudoleukaemic forms of tuberculosis we have to deal with a variety of tubercle bacillus that differs somewhat from the one ordinarily infecting human beings. Such an hypothesis could only be regarded as established if in a sufficient number of cases certain peculiarities were observed in the cultural and pathogenic character of the tubercle bacilli obtained from them that were constant, and it is needless to say that no such studies have as yet been made. In fact, Case IV. of my series is the only one, so far as I know, from which cultures have been obtained.

When I began to prepare this paper it was my object to find some common clinical features in these cases that would render possible during life their differentiation on the one hand

from cases of true pseudoleukæmia, if such actually exist, and, on the other, from cases of ordinary tuberculosis of the lymph glands. I now have grave doubts whether any such clinical differentiation is possible. Yet from the data at hand the following symptoms appear to be usually present in the forms which have certainly been determined to be tuberculous. Fever, continuous, irregular or recurrent. In fact, the forms described originally by Gowers: moderate anæmia, more frequently associated with leucopænia than with leucocytosis; progressive emaciation; enlargement of the spleen and less frequently of the liver; frequently enlargement of the superficial lymph glands, and occasionally the physical signs of enlargement of the thoracic and abdominal lymph glands; tenderness over the abdomen, especially in the right hypochondriac region; hemorrhagic diathesis, or at least a very pronounced tendency to epistaxis; albuminuria, and as a terminal symptom, anasarca, jaundice, ascites and death. Death apparently occurs in many instances as a result of an eruption of miliary tubercles. Not infrequently in these cases the following conditions occur and may be regarded as contributory evidence. Signs of pericardial adhesion and of myocardial involvement; painless, fluctuating tumors arising from the thoracic cavity and lying between the skin and the ribs; the signs and symptoms of mediastinal tumor. Of course, the presence of tubercle bacilli in the sputum or other discharges must be regarded as highly significant. Excision of enlarged superficial glands with either histological examination or inoculations into animals may confirm the diagnosis, and in some cases injections of tuberculin may give rise to the characteristic reaction, although in Case II. of my series 5 mg. of an active preparation produced rather a depression than an elevation in the temperature.

In conclusion, then, it can only be said that the time has not yet come for any dogmatic statement upon this question. None of the evidence hitherto presented can be regarded as decisive, and yet as Pinkus says, the gradual accumulation of positive evidence and the absence of entirely satisfactory negative evidence rather tend to confirm the supposition that the majority of cases of pseudoleukæmia, if not all, will ultimately be recognized as tuberculous in nature.

## DISCUSSION.

DR. WILLIAM OSLER: The subject is one in which I am particularly interested. I would first like to congratulate Dr. Sailer upon bringing this subject before the profession in this way. I think that the term "Sternberg's disease" should be so used as to exclude all cases of lymphatic tuberculosis. Long before Sternberg was born cases of general tuberculous adenitis were recognized and described as perfectly characteristic and altogether apart from Hodgkin's disease; indeed, the probability is that certain of Hodgkin's cases were general tubercular adenitis as we recognize tuberculosis. The interesting point is that Sternberg has shown that certain of this class of cases, which we regard clinically as Hodgkin's disease, and which have all the ordinary clinical, anatomical, and histological pictures of Hodgkin's disease, turn out to be tuberculosis. I think a differentiation can be made between those cases and certain cases which all clinicians have recognized as a general tuberculous adenitis. The records of Blockley contain numerous instances in which tuberculosis, such as can be recognized pathologically, has occurred in the lymphatic glands only. I remember showing to the Pathological Society a remarkable case in which there was no question as to the ordinary tubercular character of it. The lymph glands only were tuberculous. In certain of these instances the tuberculosis is confined to the lymph glands. It is met with frequently in young children, and in colored people. Dr. Sailer's paper calling attention to this subject is valuable in the clinical descriptions which give the picture of Hodgkin's disease, with the general enlargement of the glands, some cases without much fever, and a certain number that show recurrent fever of two weeks' duration and in which anatomically the process is tuberculous. To the ordinary eye it does not appear to be a tuberculous lesion. I think we shall be able to differentiate between those cases and the old fashioned cases of general tuberculous adenitis. I hold that there is a true Hodgkin's disease apart from this Sternberg variety, which has the associated tubercular bacilli.

DR. MUSSER: In looking up the subject from a different stand-point from that of Dr. Sailer I have come to the conclusion that Hodgkin's disease was practically, in a large number of cases, lymphatic tuberculosis. A case under my care during the year, and one three years ago, presented fever, recurrent in type, the so-called Ebstein's fever. It has seemed to me that all cases of Ebstein's disease were cases of lymphatic tuberculosis, and from this that lymphatic tuberculosis was probably Hodgkin's disease.

I have grown so skeptical as to the other form of Hodgkin's disease that I am glad to hear Dr. Osler hold us to the general description of Hodgkin's disease. Nevertheless, cases histologically and bacteriologically investigated

recently of so-called Hodgkin's disease are really those of lymphatic tuberculosis.

DR. ALFRED STENGEL: I would like to speak of a case now under my observation that bears upon this subject. It is the case of a woman who presents enlargements of the lymphatic glands of the anterior and posterior cervical groups, also some enlargements in the axillæ and groin. The glands are only of moderate size, are movable and do not tend to soften or conglomerate. There is certainly no tuberculosis of the lungs as far as can be determined by physical examination. The case does not present the appearances of ordinary tuberculous adenitis, nor to a marked degree of Hodgkin's disease, but from a knowledge of the contributions that have been made in this line of study, I tested with tuberculin, and the patient reacted promptly. In this way the diagnosis of generalized tuberculous adenitis was reached. One of the small nodules was removed, sections were made, and the histological features of tuberculosis and tubercle bacilli were found. The case differs from those well-known cases of manifest lymphatic tuberculosis referred to by Dr. Osler. It differs also from Hodgkin's disease in the histological and clinical manifestations. Such cases, however interesting, are not important in connection with the subject under discussion.

The question at issue is to determine whether, as mentioned by Dr. Osler, there is a Hodgkin's disease in the old sense. Is there a pathological process which is more or less related to leukaemia clinically and pathologically, which is not in the ordinary histological or pathological sense tuberculous, and which is nevertheless caused by the tubercle bacillus? In reviewing the literature of diseases of the blood a few years ago, after referring to the paper of Brentano and Tangl, I remember calling attention to the possibility of terminal tuberculous infection in Hodgkin's disease as an explanation of the occasional discovery of the tubercle bacilli in the glands in this disease. Some time after that, when I made a second review of the literature, I was forced to the conclusion that the discovery of tubercle bacilli in some cases did not suffice to prove that the process even in these cases was necessarily tuberculous, but suggested that such cases might be instances of lymphoma secondarily infected with the tubercle bacilli, these finding in the lymphomatous gland a place of lessened resistance. No one has suggested that leukaemia is tuberculous, and I believe that no one can review the literature of leukaemia and pseudoleukaemia without believing that there is a close connection between these two processes. If these views are warranted there must be a form of Hodgkin's disease which is not tuberculous. If it be true that leukaemia is not a tuberculous process we must admit that there is a form of Hodgkin's disease not tuberculous. There is a tendency in some quarters to regard all cases of Hodgkin's disease as tuberculous and to place the burden of proof on those who hold to older views and who have failed to find evidences of tuberculosis. I believe the



proper way to approach this subject is rather to expect more of proof from those who maintain that Hodgkin's disease is always tuberculous. In these remarks I am, of course, referring only to cases presenting the clinical and histological features of Hodgkin's disease and not to ordinary cases of generalized lymphatic tuberculosis, a condition well known and not now under discussion.

DR. JAMES TYSON: It appeared to me while listening to Dr. Sailer's paper there was an absence in the clinical histories of the more superficial gland involvement which I had thought characteristic of Hodgkin's disease, particularly that of the glands of the groin and the axilla. This has always seemed to me a distinctive feature. I admit that the case just reported by Dr. Stengel has rather upturned my previous conception that there is not in this general tuberculosis such a general superficial glandular involvement as he described in connection with his case. It would appear, however, that this question admits of solution in the near future, with the aid of the tuberculin test, if the estimate I have placed on its value is not erroneous.

DR. SAILER, in closing the discussion, said: I want to express my agreement with Drs. Osler and Stengel that the cases in Sternberg's study and the cases that I have collected from literature and those which I have observed myself are not cases of tuberculosis in the old sense of the word—that is, chronic tuberculous disease of the glands undergoing caseation and suppuration. In the cases that I report the glands were quite atypical, not softened, but hard and fibrous. In a letter received from Dr. McFarland it was stated that the glands in Case No. 3 had the appearance that would have caused a pathologist of the older school to diagnose the condition fibrosarcoma and not tuberculosis.

The question of Ebstein's disease I think will be decided in accordance with the view of Dr. Musser, that it is purely a tuberculous process.

I would call Dr. Stengel's attention to the fact that in the past six months, in an article published in the *American Journal of the Medical Sciences*, there was reported a case of leukaemia in which tuberculosis was demonstrated. There have also been a number of these cases recorded in the literature, with marked leucocytosis, giving rise to the syndrome of leukaemia. I cannot tell just how closely the blood changes resemble those of ordinary leukaemia.

As to etiology, ten years ago clinicians would have scouted the idea of the tuberculous origin of the syndrome of Hodgkin's disease. To-day the boot is entirely on the other leg; clinicians who still believe in non-tuberculous Hodgkin's disease are obliged to defend their position. When we compare the evidence at hand and include only those cases that have been studied with sufficient care to enable us to determine the existence or absence of tubercle bacilli, it will be admitted that the evidence in favor of the tuberculous origin of the disease is so much greater than the evidence against the tuberculous origin of the disease that we are compelled to regard



with considerable respect the opinion of those men: and, Dr. Stengel to the contrary, I must say that a careful study of the literature has led me to infer that the men are few and far between who contend that Hodgkin's disease in the ordinarily accepted sense is not really the manifestation of some unusual form of tuberculosis.

I hope that if anyone has such a case of Hodgkin's disease he will have cultures made in order to determine just what peculiarity of the tubercle bacillus causes this extraordinary alteration in the histological features of the tissues.

I think the paper of Lartigau will lead to important developments in regard to the tubercle bacilli.

## RECENT VIEWS OF THE ORIGIN AND NATURE OF HERPES ZOSTER.

By ARTHUR VAN HARLINGEN, M.D.

[Read December 4, 1901.]

SOME years ago my friend Dr. Curtin called my attention to some cases observed by him, which seemed to point to the occurrence of herpes zoster on the pleura, the peritoneum, and in the articulations. He asked me whether I knew of any similar cases. I had not had any personal experience, but determined to examine the literature of herpes zoster with this point in view. It is only recently that I have had the opportunity of doing this, but, although references to the subject are scanty, quite a number of cases have been published which go to confirm Dr. Curtin's observations.

At the same time I have found so much of interest in scattered monographs of recent date that I have thought well to give some account of the views generally prevalent among dermatologists and neurologists regarding the nature of herpes zoster.<sup>1</sup> In order to do this satisfactorily, it seems desirable to give a hasty sketch of what is known regarding the pathology of the disease and of the various theories as to its origin.

Barth, in an account of herpes zoster, or, as I shall call it for convenience, zoster, says that Parrot, in 1857, advanced the theory of zoster as a secondary disease, subordinate to a neuralgia; and Charcot, in 1859, called attention to a case, the first recorded, where zoster followed an injury. In 1861 Bärensprung, in his classical paper, developed the idea of the nervous origin of zoster, and attrib-

<sup>1</sup> Dr. Curtin's views are stated in several monographs. "Is Herpes Zoster a Cause of Pleurisy and Peritonitis?" *Sanatarian*, December, 1890, and in other publications.

uted it to a disease of the ganglionic system, an irritation of the spinal ganglia, or of the Gasserian ganglia, while admitting that peripheral irritation of a nerve might result in a limited outbreak of the eruption.

In 1864 Mitchell, Morehouse, and Keen showed that irritation and not section of a nerve was the cause of zoster and similar eruptions. Later it was shown that compression by tumors, etc., might result in zoster on the distribution of the implicated nerve.

In 1872 Charcot reported a case of double zoster of the trunk following acute myelitis of the anterior cornua, and later reported cases of zoster occurring in connection with locomotor ataxia.

The mode of action of the morbid influence through the nerves on the skin was early made the subject of speculation, and several theories have been brought forward. What was known as the *vaso-motor theory* assumed that the contraction, expansion, or paralysis of bloodvessels, and the consequent increase or decrease in the amount of nourishment brought to the cells, might lead to nutritive changes. This failed of experimental proof.

Samuel suggested a theory of *trophic nerve fibres* which was ingenious, but the existence of such fibres never having been proved, the theory fell to the ground.

The theory of the *trophic action of sensory nerves* attributes to the ordinary sensory and motor nerve fibres those functions for which Samuel had provided a special group of nerves. The nervous system acts on the nutrition of the anatomical elements by maintaining their functional activity. Trophic influence is thus transmitted to the skin and mucous membranes by the sensory nerves. Any alteration in the sensory fibres would result in the enfeeblement of the trophic influence of spinal and Gasserian ganglia upon these fibres and probably through their mediation on certain elements of the skin itself.

If this is the case we must admit that the weakening of this trophic influence would create a state of least resistance, or of greater vulnerability in those parts of the skin connected with the peripheral extremities of the affected sensory nerves.

Under these conditions an irritant local cause, such as pressure, rubbing of the skin by clothing, or even contact of the air, might

determine the appearance of the herpetic eruption, and, as would appear from recent observations, a microbic invasion could also occur.

Although this theory is attractive, and, if well founded, would explain the pathology of zoster better than any yet brought forward, it has not as yet been proved, and remains a theory like the others.

The simplest and most plausible theory of the production of zoster, and one, indeed, which must account for a certain number of cases, is that of *propagated neuritis*. This supposes that zoster is simply the result of an inflammatory irritation transmitted by continuity of tissue from a nerve twig, or branch, to the cutaneous elements among which it is distributed.

I may say here in passing that these theories take for granted that all zosteriform eruptions are of the same nature, and that each belongs to a specific affection: herpes zoster. In the present state of our knowledge, however, this is by no means universally admitted. We may have a specific herpes zoster, as we believe there is a specific pemphigus, while at the same time we may have various zosteroid eruptions, as we have various bullar or pemphigoid eruptions, which may arise from various causes.

Such, at least, is the generally prevalent belief among the dermatologists of to-day.

At the time Barth wrote, discussions upon the etiology and pathology of zoster seemed premature. Zoster was to be recognized as the cutaneous expression of a nervous disturbance, irritative in character, affecting sometimes the peripheral sensory nerves, and sometimes the spinal and cranial ganglia. Sometimes resulting from an injury, as contusion or compression of a nerve: sometimes as the result of cold, or under the influence of a general perturbation of the system.

The nerve disturbance might at times be so slight as not to affect perceptibly the anatomical integrity or the functions of the nerve fibres, and might show itself only by the cutaneous eruption.

At other times, however, and especially in the old, this slight initial disturbance might precede a destructive neuritis, which might give rise to anæsthesia, rebellious neuralgias, and various other disorders of sensation so common as the result of severe zoster.

Although, most commonly, the morbid process produces only slight skin lesions, the irritation might extend to other organs innervated by the same nerves, and might determine grave and irreparable disorders. Ulceration of the cornea, as observed by Hutchinson and Hybord many years ago, and which is an occasional accompaniment of ophthalmic zoster, was one of the first of these complications to attract attention. Jouffroy pointed out that the neuritis of zoster may be propagated to neighboring nerves, and may cause atrophy of certain muscles. Such was the position of the zoster question as stated by Barth in his article, to which reference has been made. He, however, hazarded the suggestion that visceral organs might be attacked under the influence of the same cause as that producing the zoster in a given case, and referred to the opinion of Fernet, that certain pneumonias may be the expression of a sort of zoster of the pneumogastric nerve.

This prophecy, put forth by Barth twenty years ago, has been verified by subsequent clinical observations. A large number of cases of visceral disorders of various kinds in connection with zoster have been reported of late years. Pitres and Vaillard, Leroux, Potain, Huchard, Chandeaux, Mongour and Michel, Cantrell, Curtin, and others have shown the concurrence of zoster with tuberculosis, pleurisy, peritonitis, etc. Palm reported the case of an infant with bilateral zoster of the third branch of the trigeminal, which developed on the third day of a follicular angina. Hervouet reported a case of cervicobrachial zoster, accompanied by paresis of the arm, and, in addition, incomplete facial paralysis and ptosis. The various symptoms occurred simultaneously and, as will be observed, in different nerve tracts.

While these and similar cases continued to appear, other observations were published, going to show a close connection between zoster and various infective diseases. Gaucher and Barbe wrote on zoniform syphilides, Jullien on zona and syphilis, and Spillman and Etienne published observations of a similar character. In the cases reported by the first of these writers, the distribution, as I understand, rather than the character of the lesions, lead to its denomination of zoniform; but the point of interest lies in the suggestion of the authors that the lesion had been produced, in all

probability, under the influence of the pathogenic agent of syphilis or of its toxin upon the spinal axis.

Cancer, otherwise than through the direct influence of pressure from the new growth, has been suggested as a cause of zoster. Carrière, in a case of femoro-cutaneous zoster following cancer of the uterus, found parenchymatous neuritis of the nerve involved. There was no cancerous infiltration of the nerve, and Carrière attributed the neuritis to the local and direct action of cancer toxins. One of Dr. Curtin's cases was also connected with cancer of the œsophagus.

The occurrence of zoster in connection with coal-gas poisoning and as a result of the administration of arsenic presents certain problems which have not been studied with sufficient care to enable us to express any opinion. The fact that zoster or zosteriform eruptions may occur under such circumstances is established, but more cannot be said.

Wasilewsky, in his monograph on zoster as an infectious disease, cites reports of epidemics of the affection. He regards the question of immunity as settled, but with the numerous cases of recurrent zoster reported of late years, it is difficult to agree with him on this question, unless, indeed, we come to recognize the recurrent cases as zosteroid in character, rather than as true zoster.

In typical cases, prodromata, as gastric disturbance, and fever appearing several days before the eruption, with a temperature often reaching 104° F., and ceasing with the outbreak of the eruption, point, in Wasilewsky's opinion, to an infectious origin for the disease, and this view is supported by the observations of Head and Campbell, which I shall cite later.

A point in favor of the infectious character of zoster is the occurrence of enlarged lymphatic glands. Grindon and Hay have shown that true zoster is always preceded by adenopathy in the neighborhood of the eruption, or even by generalized involvement of the lymphatic glands. Hay discovered cocci in the glands.

The infectious nature of zoster having been so strongly indicated by the observations of numerous writers, it is not surprising that facts should now begin to appear in favor of its contagious character. Ferré has reported some very interesting cases in this connection. Ferré

thinks that in some cases zoster may be the consequence of a meningeal or spinal affection, and in the epidemic form may be an indication (*symptôme révélateur*) of an attenuated form of cerebro-spinal meningitis. As numerous instances of the recurrence of zoster have been reported of late years, these must be taken into consideration before the infective theory is generally accepted. The view that there are several varieties of zoster, or that there is one specific zoster, an infective disease, and, therefore, not recurrent, and various zosteroid eruptions due to different causes, is one that seems to have gained considerable adherence of late years, and in the light of recent observations is certainly a plausible explanation of numerous otherwise anomalous phenomena.

The anatomy of the lesions of zoster themselves has been made the subject of investigation in the light of more recent knowledge and with the aid of modern methods. Peffer maintains that the true cause of zoster is in all cases a protozoid, which he has found in the affected skin and has described. Hartzel, who has made similar investigations, says that these protozooids are not present in ordinary inflammations of the skin, but are peculiar to zoster, variola, vaccinia, and varicella. Gilchrist, after an elaborate investigation of the subject, concludes, however, that the so-called protozooids are really the nuclei of epithelial cells.

Up to within the past year or two, Bärensprung's observations and conclusions have never been questioned, and zoster has everywhere been received as an affection closely connected with the sensory nerves, and following in its occurrence the distribution of these nerves in the skin.

It cannot have failed, however, to strike the careful observer that the eruption of zoster does not invariably follow the line of distribution of the nerves, this circumstance being particularly noticeable in thoracic zoster. Brissaud, a recent writer, goes so far as to assert that in a large number of cases the concordance of the eruption of zoster with a nerve path is a fiction.

Having made the same observation with regard to other diseases besides zoster, Brissaud sought for an explanation and found it in the theory of "metamerism."

Concluding from our knowledge of embryology that the spinal



cord is composed of a series of segments superposed and relatively independent (metamers). Brissaud attempted to prove that the eruption of zoster should appear in the territory of a region innervated by a medullary metamer. This territory of innervation, however, is sometimes entirely different from that which corresponds simply to the course and distribution of the sensory nerve fibres.

Another and quite different theory of the relation of the zoster eruption to the nervous system has been proposed by Abadie. He maintains that the skin affection does not result from an alteration of the peripheral sensitive nerve fibres, nor from a medullary lesion, but from a pathological condition of the arteries and of the vasomotor nerves which regulate their dilatation in the region where the eruption is situated.

In a general way the sensory nerves accompany the arteries, at least during a portion of their course, and, therefore, the zoster eruption, which really occupies the territory of vascular distribution, has heretofore been supposed to occupy the nerve territory. As, however, in certain localities, these two territories are neither identical nor superposable, apparent anomalies supervene, anomalies which Brissaud tries to explain by his "metameric" theory above mentioned. This hypothesis is not necessary, however, to explain the topographical anomalies of the eruption, as the cutaneous lesions occur along the bloodvessels and not along the nerve filaments.

Taking ophthalmic zoster as an example, Abadie asks how it is, if zoster is due to inflammation of the trigeminal nerve, that it only occurs (save in the very rarest cases) in the first or ophthalmic branch. As a fact, maintains Abadie, the eruption extends over the area supplied by the *supra-orbital*, *frontal*, and sometimes the *nasal* arteries.

The lesions of zoster, says Abadie, are due to a trophic influence proceeding from the *sympathetic nerve fibres*, which in the case of ophthalmic zoster, follow the course of the arteries just mentioned. The pain and other nervous symptoms, which may or may not accompany the eruptions, are due to some involvement of the sensory nerves, which may be implicated in one case and may not in another.

This theory is supported by the form of the eruption in thoracic

zoster. This does not occur above the line of the third intercostal space. The arteries supplying the three upper intercostal regions, instead of proceeding from the aorta, are derived from the subclavian artery, and consequently their vascular origin and that of the vasomotors which accompany them are different from the others which come directly from the aorta.

This theory of Abadie's makes clear, so he says, the apparent anomalies of the eruption which are inexplicable otherwise, but it takes away from the sensitive nerves of relation a part which does not belong to them and assigns it to the great sympathetic. It proves that the latter really commands and regulates nutrition in all the regions to which it is distributed, whether visceral or cutaneous.

We may thus understand, also, that certain forms of ophthalmic zoster may present particularly grave cerebral complications, and may be accompanied by hemiplegia, as Brissaud has shown, in some cases. The mechanism of these lesions has been difficult to explain by the nerve theory, but it is easily understood by accepting the excessive vasomotor dilatation of certain cerebral arterioles which may provoke rupture in their territories of irrigation. Finally, Abadie says that quinine is a specific in ophthalmic zoster. Now, quinine is essentially a vasoconstrictor medicine acting on the sympathetic and producing a constriction of the arterial vessels.

These views of Abadie have not been generally accepted, although there is certainly something in them. But, as Hallopeau says, the character of the concomitant and consecutive pains appear necessarily to imply a participation of the sensory nerves, and also the localizations can only be explained by a metameric action.

The blood examinations which have been made in zoster are worthy of mention, although their significance is not apparent. Like the microscopical examinations of the lesions, they are materials of possible future structures, but have not yet been fitted into their place.

Leredde says the white globules may fall to 3500. The polynuclears are diminished to 45 per cent. on an average; they may fall to 37 per cent. On the tenth to the twelfth day an eosinophilia of 6 to 8 per cent. has been noted.

Head and Campbell, in a recent and extremely elaborate paper,

give a large number of facts regarding the origin and distribution of zoster. These investigators have been able to map out the affected areas in zoster, and have subsequently examined the spinal cord and nerves implicated. The cases in which they have been able to make post-mortem examinations number more than the sum total of those previously recorded by all other observers.

Head and Campbell find inflammatory and destructive changes in the posterior ganglia of the cord and in the Gasserian ganglion, and degeneration in the nerves leading to the skin. In mild cases the effects of these changes gradually pass away, but in severe cases the nerve fibres that have degenerated are replaced by fibrous tissue, and whole bundles of the nerve may be sclerosed. Degeneration in the spinal cord occurs secondary to the herpetic lesion of the ganglion. It may be noted, referring to the brain symptoms in connection with ophthalmic zoster, that the third division of the trigeminal is connected with cells in the Gasserian ganglion which send fibres centralward to lie in the so-called ascending or spinal roots.

Head and Campbell conclude that some agent, the nature of which we are ignorant, chooses the substance of the posterior root ganglion for its selected activity, producing profound inflammatory changes. These destructive changes in the ganglion give rise to irritation of its nerve elements, and to this irritation is due the eruption on the skin. Acute inflammation of a posterior root ganglion, due to its implication in some local inflammatory process, can apparently produce an herpetic eruption indistinguishable from an eruption which arises as a manifestation of the acute specific disease (as, for instance, a case of zoster reported by Head and Campbell, where lymphosarcoma invaded the posterior root ganglion directly).

Zoster may appear in the course of gross organic disease of the spinal cord and roots. In some such cases Head thinks the original disease simply predisposes to an attack by the specific agent supposed to be the chief etiological factor in the production of the zoster. Head has traced nerve twigs up to the portion of skin excised for examination, and found they show marked signs of degeneration. He did not succeed in demonstrating degenerated fibres in the actual portion of skin examined.

A typical attack of zoster arises without any obvious peripheral

or cerebral cause, and, as has been said, must be considered an acute specific disease of the nervous system, for it starts with a prodromal period of varying length, during which the temperature is raised. During this period the patient feels ill and has more or less pain.

If a child, he may be supposed to be sickening from one of the ordinary specific diseases. Then the rash appears, the febrile period lasting three to five days. Head's experience with recurrent zoster is also worth noting. He met with but four cases of relapse in four hundred cases of zoster.

In connection with the occurrence of zoster as a specific infectious disease we must consider the large number of zoster-like eruptions evidently due to various causes, as injuries, poisoning by arsenic, coal gas, etc. All these must be ruled out from the division of true zoster. On the other hand, the occurrence of zoster as a specific fever running a regular course and characterized by a typical eruption, prepares the mind for the reception of Curtin's theory as to the involvement of various membranes and viscera.

If the cause of zoster lies in a disorganization of certain nerve cells or nerve fibres by the toxin of a specific germ, or by an unknown agent of any kind, there is some reason for admitting the possibility that the same agent may give rise to inflammatory symptoms in the pleura or in the articular cavities. As Osler and others have described the various visceral complications of erythema multiforme, so we may regard the cases observed by Curtin as those of visceral complications of herpes zoster, and I have no doubt that when the attention of observers has been drawn to this aspect of the case we shall find numerous cases of such complications reported.

CONCLUSIONS. From what has preceded, the following conclusions may be drawn :

1. Under the designation *Zoster* or *Herpes Zoster* is to be understood a specific infectious, and possibly contagious, exanthem, characterized in its invasion by lassitude, general malaise, chills, increased temperature, and more or less digestive disturbance.

Following this, in most cases, neuralgic pains are experienced along certain nerve paths or metameric areas, together with the development of enlarged lymphatic glands.

After a period of several days, more or less, during which the symptoms mentioned, or some of them, have manifested themselves, the characteristic exanthem shows itself, and runs through a fixed cycle of development, acme, and decrudescence. The general symptoms, particularly the neuralgic pains, may continue during this period, or, in many cases, may diminish, usually disappearing with the eruption. In other instances, and particularly in older persons, the neuralgia may form a prolonged succedaneum to the regular course of the disease.

In a certain number of cases, probably however rare, various visceral complications may accompany the affection. Such are paralysis of sensory or motor nerves, inflammations of the pleura, peritoneum, articulations, or viscera.

2. The infection attacks chiefly the posterior (sensory) ganglia of the cord and the Gasserian ganglion. From thence inflammation and degeneration may extend along the nerve trunks and fibres.

No other lesions have as yet been discovered post-mortem, although it is probable that further observation will result in tracing the disease in the various membranes and viscera when its presence has been clinically noted.

The numerous examinations of the skin lesions and such blood examinations as have been made have not as yet thrown any light upon the nature of the disease.

3. Zosteroid eruptions are not infrequently observed in cases of poisoning from coal gas, after the ingestion of arsenic, following injuries of the nerves, as a result of moral shock, as grief, or in hysteria, and probably under other conditions. These, however, are to be distinguished from the true herpes zoster as defined above.

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## DISCUSSION.

DR. HARTZELL: The subject is one in which I have long been interested. There are two etiologically different kinds of disease included under the name of zoster. There is abundant evidence to show that a zoster-like eruption may follow injury to a nerve, many cases following traumatism having been reported. I had under observation myself some years ago the case of a man who, after fracture of the femur, suffered very many attacks of eruption over the course of the sciatic nerve, which was indistinguishable from the ordinary eruption of herpes zoster. In this case there were many recurrences. As is well known, second attacks of zoster are rare. Notwithstanding that a considerable number of such cases have been reported in recent years, it is nevertheless a fact that, in comparison with a number of cases, second attacks are uncommon. Some ten years ago I looked up the matter of recurrent herpes zoster, and I was only able to find ten or twelve cases on record. That, of course, did not represent the actual number of cases in which second attacks occurred.

As to the infectious nature of the disease, I am convinced that there is a form due to infection. Many cases present all the symptoms of an infectious disease. The fact that one attack confers immunity is extremely suggestive in this direction. The disease is a self-limited one; it occurs in epidemics; and in a few instances, at least, the evidences of contagion have been well marked. Some years ago Pfeifer described certain bodies which he found in the lesions of herpes zoster, similar bodies being found in the vesicles of varicella and vaccinia. I myself, some years ago, examined many of the lesions of herpes zoster, and I was quite confident that many of the bodies which Pfeifer described as protozoa were forms of cell-degeneration. Indeed, at that time I was inclined to believe all the peculiar bodies Pfeifer referred to and with which he illustrated his monograph

on protozoa were in reality forms of epithelial degeneration, but I am not so certain of that at present. There are certain bodies in the lesions of herpes zoster which are due to hyaline degeneration or some other degeneration of epithelial cells, but not all of these peculiar structures can be accounted for in this way. Very recently Funk has described similar bodies as occurring in the lesions of vaccinia; and Wasilewsky, who has worked out the subject with the greatest thoroughness, is confident that certain bodies in the lesions of vaccinia are micro-organisms. I think it is likely that in the cases of herpes zoster distinguished by a single attack, in which no traumatism of the nerve or no nerve disease can be demonstrated, some infectious agent is the cause of the disease, and that this may be some one of the protozoa. Of course, this has not been proved. Our technique is such that we are unable to distinguish these organisms with any certainty. The whole subject is one of extreme interest and importance, owing, in part, to the close resemblance which the peculiar bodies found in the lesions of zoster, variola, and varicella bear to one another.

DR. CURTIN: The subject of Dr. Van Harlingen's paper is one in which I have been much interested for many years.

In 1890, before the American Climatological Association, in session at Denver, Colorado, I presented a paper with the title "Are Pleurisy and Peritonitis Causes of Herpes Zoster?" (*Transactions of the American Climatological Association*, 1890), and Dr. Van Harlingen has alluded to another, dealing with the relation between herpes zoster and internal inflammations (*Philadelphia Hospital Reports*, 1900).

The observations embodied in these papers extend over a period of fifteen years, during which time I have seen the affection occur in phthisis quite a number of times; in pneumonia twice, in pleurisy twice, the eruption making its appearance after the occurrence of effusion; in meningitis once, in peritonitis once, with the eruption directly over the area of inflammation; in cancer of the œsophagus once, in arthritis of the knee once, here also appearing after the occurrence of an effusion, after abortion, and many times in influenzal catarrhal fever.

As to its being caused by toxæmia, I am inclined to think that such a view is tenable, from the fact that it has occurred so frequently in connection with influenza. During the first year that the grippe was epidemic I collected eleven cases of herpes zoster occurring after apparently quite insignificant attacks of that disease. This in itself would seem to indicate that the association was *propter hoc* rather than *post hoc*, the primary disease either exciting an associated poison, or predisposing in some other way hard to explain.

I am very glad that Dr. Van Harlingen has written his paper. He has thrown much light on the history and etiology of the subject.



## ASSOCIATION OF HYSTERIA WITH INSANITY.

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[Read December 4, 1901.]

THE relation of hysteria and the various forms of insanity is in some measure twofold: first, the insanity having hysteria associated with it; and secondly, hysteria in which insanity complicates. These borderland distinctions are not always easy to differentiate, but are very important to separate, since the medical jurisprudence and prognosis of the case will depend upon the right interpretation.

In this short paper it is, therefore, the writer's intention not to dwell upon the diseases, insanity and hysteria, separately, but of those associations of the two which are the more confusing to the physician. Granting that hysteria is not, in the true sense, mental alienation in the vast majority of instances, it would seem better to keep clear of the phrase "hysterical insanity" as applied to a minimum of cases of a *peculiar* type of insanity associated with hysteria, and, indeed, a part of it, as H. C. Wood well points out. And in these cases, from a jurisprudence point of view, we must, of course, assume responsibility of commitment to an institution, though it will be much rarer to resort to this extreme than in other cases of mental disease. Dr. Folsom, quoted by Wood, gives a very lucid description of "hysterical insanity," which, like the bizarre hysteria as usually seen in any other of its protean manifestations, whether of special sense, of sensory, or of motor disturbance, or of simulation of organic disease, as shown in this mental type of the queer psychosis in question, to wit: Folsom says hysterical insanity "is characterized by extreme and rapid mobility of the mental symptoms—amnesia, ex-

hilaration, melancholic depression, theatrical display, suspicion, distrust, prejudice, a curious combination of truth and more or less unconscious deception, with periods of mental clearness and sound judgment, which are often of greater degree than is common in their families: sleeplessness, grotesque and distressing hallucinations of sight, distortion and perversion of facts rather than definite delusions, visions, hyperæsthesias, anæsthesias, paræsthesias—abortive or sensational suicidal manœuvres, occasional outbursts of violence, a curious combination of unspeakable wretchedness alternating with joy, generosity, selfishness—of gifts and graces on the one hand, and exactions on the other. One such person in the house wears out and outlives, one after another, every healthy member of the family who is unwisely allowed to devote herself with conscientious zeal to the invalid.”

The writer has a case of hysteria under his care at the present time, in a young woman, aged seventeen years, who has been of good intellect, perhaps the brightest of a family containing seven children. During the past four years she has had one or two attacks in which she becomes secretive, goes without food for several days at a time, in the last attack of which, beginning in January, 1901, the condition of depression was associated with hysterical outbursts of crying, although she never had a convulsion. Four weeks previous to coming under my care in November last, she suddenly, while in the picture of physical health, began to go without food, which, her family asserts, was kept up for eight days: she imagined also that the X-rays had been used upon her and had burned her; that blood had been taken from her head, and that it had been “sewed up,” and she was surely going to die. She persisted in taking no food in spite of family solicitations and of her physician, Dr. W. F. Haines, of Seaford, Del. A week previous to her coming to Philadelphia she began to expectorate large quantities of blood-tinged mucus. We could get no speech from her, the patient casting her eyes in disdain toward the doctor and nurse, occasionally answering a persistent question in monosyllables. She had become physically wasted and anæmic. (Hæmoglobin, 80 per cent.; red blood corpuscles, 3,800,000.)

Isolation from her family, forced feeding through the stomach-

tube, static electricity, with massage, have greatly improved her physical condition. Occasionally she will have an outburst of temper, only to relapse into apparently studied depression. It should be stated that there is no history of hereditary mental disease in her family. The absence of a true dementia in the symptomatology, but rather of the pseudo-melancholia described, makes us place the patient in the category of hysterical insanity, and that the hope for cure will come through physical betterment and morale. While she has never shown suicidal tendencies, nor do I believe she would take her life, at the same time it may be advisable to place such a patient in an institution for mind diseases, which may tend more than anything else to arouse her conscience to the fact that she can help herself.

Dr. S. Weir Mitchell has given us the most comprehensive *régimé* for the successful management of hysterical disease. It is not the purpose of this paper to rehearse treatment.

Having studied and reported a case of this hybrid disease (hysterical insanity), the more unusual psychosis, we should like to give a few facts, even if not new, which will aid in the diagnosis between the (*a*) hysteria complicated by insanity, and (*b*) insanity associated with the previous hysteria, as mentioned in the beginning. The most difficult pure mental disease to distinguish from hysterical insanity is hebephrenia, or the paraneic insanity of adolescence so-called. In this there may be physical signs of degeneracy. When these are absent the mental symptoms alone will be, perhaps, diagnostic—*i. e.*, excitation of the depressive emotions in the form of a dementia rather than melancholia will prevail as the type of alienation, the patient being more disposed to wander away from home, to show no systematized studied desire to annoy her caretakers, and, withal, to show especially the lack of moral responsibility.

In a paper read before this College in January, 1900, what we considered a typical example of the latter form of mental alienation, which was diagnosed from hysteria by the differential points given above, seemed pretty clearly to be complicated at least by intestinal auto-intoxication, so that antiseptic treatment directed toward the alimentary canal was a measure added as an adjunct to forced feeding that cured the patient, if we may call it such, since no relapse

has taken place in over two years. Intestinal antiseptics in the case reported to night has seemed to better the physical state, for she is gaining weight, and pallor is giving way to a pink skin.

Hysteria as a clinical entity may develop, as is well known, beyond the essential stigmata of this psychosis, three aspects: first, the emotional element more particularly; secondly, the physical state, such as paralysis, sensory or motor; and thirdly, the clinical side may be specially shown in disturbance of organs such as the heart, stomach, etc. In our experience this first subdivision—that is, of hysteria without physical or objective symptoms—is the type that may be complicated more frequently by insanity of one form or another, and this is usually a form of mania. Such a case we have recently seen, where the mania with delusions followed pronounced hysteria due to overwork, the patient having been hysterical long before insanity set in. Forms of delusional insanity of slow onset in the hysterical subject are more likely to occur, however, where the mind is given suggestion by some physical defect, as in cases of hysteria with anæsthesia or a motor palsy in the symptom complex. The autosuggestion through the paralysis mentioned on the hysterically enfeebled mind may produce, therefore, a true delusional insanity which may be quite intractable after recovery of all other evidences of hysteria *per se*. This is also true of the hysterical cases of the third group—that is, with symptoms referable to various organs of the body and in proportion as hereditary influences are of a markedly neurotic kind—as, for instance, in a woman under our care at the present time who has the delusion of having cancer of the breast, even after the physical demonstration has been made of its absence, and who promptly transferred the delusion to one of the stomach during a recent attack of influenza of gastro-intestinal type. This woman is eminently hysterical, and we might say mildly, a case of delusional insanity. The heredity being good, however, if the hysteria can be cured by suggestion and general upbuilding of the system, we feel the mild delusional alienation will recover.

To make it clear that hysteria is engrafted upon an insanity is the more difficult problem. Since we are disposed to interpret confusion, delusion, or exaltation as symptoms of the mental disease, it will be practically impossible to determine hysteria established

upon a subacute mania. When it comes to melancholia or dementia, it seems to us it is impossible to distinguish a hysteria that may complicate the mental condition and produce, therefore, the picture of insanity plus hysteria. Such a state is different, as mentioned in the beginning of this short paper, from hysterical insanity, as we have tried to make plain; and distinct from hysteria plus insanity (usually a mania occurring in the hysterical subject).

This subject is thought fitting to be presented more from a prognostic point and the jurisprudence aspect, since it is often most difficult to decide when a case should be committed to an institution for the treatment of the mind: and this is the more important because the presumed stigma of being committed to an asylum does exist among the laity, so it is our duty to keep out of the asylum the case that will recover in private. We personally must weigh the family history and physical condition of the patient before committing any case of mental disease to an asylum, but we should hope to be the last not to commit the case that is likely to do injury to himself or others. Even in the case of hysterical insanity, so-called, it may be desirable to commit the patient as a *dernier ressort*. Sometimes these patients may commit suicide from mere devilishness more than from any true insanity, as in the case referred to at the outset; and if this girl does not improve we shall deem it wise to commit her to an institution within a month. The more closely we study the individual case of alienation the less easy it is to decide the prognosis, unless we *do* weigh seriously the varying symptoms (frequently confused) of that bizarre disease hysteria so frequently associated with insanity, as it has been our effort to emphasize.

If this short contribution will but stimulate a desire and endeavor to seek for the hysterical element in insanity and the close individual study of the case, it will not have been in vain. The one aspect that hysteria is apt to take in insanity, besides its well-known grotesque features, is exemplified by the entering into any case of mental disorder a large element of the personal desire to trap you, in which a patient frequently shows her hysterical mental state in the spirit best manifested by the non-medical word *disdain*.

## DISCUSSION.

DR. CHARLES K. MILLS: The subject is one, as Dr. Pearce has indicated, of great practical importance. With Dr. Mitchell, my own experience has been that the mistake is frequently made in general, and sometimes in special practice, of confusing the different forms of insanity in their earlier stages and sometimes in their fully formed stage with hysteria. The forms of real insanity which are most often mistaken for hysteria are dementia præcox (to which Dr. Pearce has alluded), acute mania, melancholia, and paranoia.

I regard the diagnosis in some of these cases as somewhat difficult, and yet there are certain fundamental facts or principles on which to base a diagnosis. The acute mania proper or the subacute mania can always probably be differentiated from hysteria by one who is familiar with both diseases. The matters of chief diagnostic importance are the presence of the well-known physical stigmata of hysteria and the peculiarity of the mental manifestations. The study of delusion is at the root of differential diagnosis of hysteria from these different forms of insanity, not only the study of well-organized and well-expressed delusion, but the study of the delusional state. Even the existence of well-defined obsessions, which are tending to fully organized delusions, will, in the absence of the usual stigmata of hysteria, enable us to say that we have not hysteria to deal with.

Dementia præcox is an affection which is not well understood, except by the alienist, and I think that seven out of eight cases almost that I see in private practice have been previously diagnosed as hysteria. In the study of a case of this sort the time at which the symptoms appear, the fact that you do not have, except in rare cases, any of the true stigmata of hysteria, the existence of a peculiar semi-delusional state and the incapacity for intellectual effort will be the guides to diagnosis. Paranoia, and especially that form which originates at the period of adolescence or just before, is very frequently supposed to be hysteria. The reason for this is clear. The patient has periods of excitement, and exhibits many of the phenomena which are popularly classed with hysteria, and some of which may belong to hysterical episodes.

I do not believe that there is much difficulty in distinguishing true melancholia from hysteria. The distinction is to be reached by a study of the patient's mind with regard to the delusional or obsessional state. There is a true hysterical mania which is not, as it is often supposed to be, ordinary acute mania. It is somewhat difficult to distinguish, and you can only make a diagnosis by a close study of the patient's history and of the well-known phenomena of hysteria.

DR. F. SAVARY PEARCE: I have not anything to add in particular reference to the subject except the point as to commitment to asylum of mental

cases. I was in one of the magistrate's offices recently and asked him if he could calculate how many cases were committed to asylums from the city of Philadelphia. He looked over his records and found that there were fifty within this year from his court, and that there were about thirty such courts in this city. Calculating on that basis, it would seem that probably 1 in 1500 or 2000 people were committed to institutions from Philadelphia as being insane. This does not particularly point to the subject, except that it shows how many cases are committed to asylums, and brings back or reinforces the statement I made in the paper, that we should try to separate hysteria, insanity, and the so-called "hysterical insanity." Hysteria and hysterical insanity being better treated (or a large majority of them) outside than in the asylum, the crowded conditions in the asylums to-day would be lessened if we made fewer mistakes in diagnosis. So the practical point, from a scientific and civic point of view, is to study this subject most carefully to see if we cannot learn something more definite, and in that way relieve the great congestions in State institutions, such as at Norristown, through lessening the number of commitments.



## ALBUMINOUS EXPECTORATION FOLLOWING THORACOCENTESIS.

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TAPPING of the chest for the removal of fluids is ordinarily such a simple and safe procedure that the possibility of serious accident scarcely ever enters the physician's mind. This feeling of security is of decided advantage, inasmuch as it ensures a desirable confidence and makes resort to aspiration more prompt and more frequent than was the custom among our predecessors, who greatly magnified the gravity of the operation—so much so, indeed, that many patients died for the want of timely tapping.

The knowledge that accidents may occasionally occur is not, however, a real handicap, for it makes us more circumspect in performing the trifling operation, and renders us unsurprised and ready when untoward circumstances arise.

It is not my purpose to review all the complications that may accompany or follow tapping of the chest, such as syncope, pulmonary and other forms of embolism, convulsions, etc. These are adequately dealt with in the articles and works of Leichtenstern, Foucart, Dandridge, and Wilson Fox. I merely intend to give an account of one particular complication, which, although exceedingly rare, has in the past aroused remarkable interest, viz., albuminous expectoration. A survey of the literature shows that this was first described by Pinault, in 1853. His patient was a man thirty-four years old, who had been suffering for three months with left-sided pleural effusion. Three litres of fluid were removed by tapping, with instant relief of the dyspnœa. In the evening of the same day, however, the shortness of breath returned, mucous râles appeared

over the chest, and the patient began to expectorate large quantities of an albuminous fluid, bringing up two cuspidorfuls—about a pint. Cases were subsequently reported by d'Éspine, in 1869; Woillez, in 1872; Marrotte, in 1872; Behier, in 1872, and Lande, in 1873. The entire subject was thoroughly reviewed in 1873 by Terrillon, who collected twenty-one observations, including his personal cases, with two fatalities.

Very little attention was bestowed upon the condition outside of France, yet it is of great interest to note that one of the first publications made elsewhere was that of Dr. William Pepper, in 1874. In a case of hydrothorax seen with Dr. T. J. Yarrow, of Philadelphia, Dr. Pepper withdrew by aspiration seventy-five ounces of serum. A troublesome cough followed, but was relieved by deodorized tincture of opium. The expectoration set in eighteen hours after the tapping and continued for twenty-four hours, the patient bringing up three gills of fluid altogether. This fluid closely resembled that removed from the chest. A dangerous syncopal attack, from which the patient was aroused by stimulants, occurred six or seven hours after the operation.

In 1873 the subject of albuminous expectoration formed the theme of a heated discussion in the Académie de Médecine and the Société médicale des Hôpitaux. This was at the time when, through the efforts of Dieulafoy and Potain, in France, and Bowditch, in this country, aspiration was coming into use, and, as a novel method of procedure, had its advocates and opponents. This discussion stimulated the publication of numerous cases, and of opinions on the etiology of the condition, and the French literature of the period contains a large number of reports, among others those of Prévost, Dujardin-Beaumetz, Moutard-Martin, Féréol, Hérard, Desnos, and Drivon, and that of Laboulbène, who was one of the first to give a careful analysis of the expectorated fluid. Cases were also reported by Dieulafoy, and later by Hayem and Tissier, and others.

In the German literature I was able to find but three cases—those of Kredel, Schütz, and Scriba, although Leichtenstern, in the article already referred to, makes comprehensive reference to the condition. Strümpell also mentions it.

In England a full report of the French discussion was published by Labbé in the *British Medical Journal* in 1873, and some obser-

vations were recorded by Johnson and by Duffin. A clear account of the subject was given by Wilson Fox in his monumental work on *Diseases of the Lungs and Pleura*. The first case reported in detail seems to have been that of Gee, in 1886, although a brief and interesting report of a case was made by Fraser, in 1876. West, Haviland Hall, and Hale White published cases in 1896.

In American literature, aside from the case of Dr. Pepper, I have found scarcely any reference to the subject. Bowditch mentions it, but I was unable to find his original publication. Systematic writers, such as Donaldson, Osler, and Whitney, refer to the subject.

The history of the case which I have had the opportunity of observing is as follows:

Miss J. R., forty-eight years of age, unmarried, born in Philadelphia, was always healthy, except for sick headaches, from which she had suffered all her life, until a year ago, when, at about the time of the menopause, they disappeared. Her mother died of dropsy at the age of sixty-two; her father is living and healthy; two sisters died at the ages of twenty-two and twenty-four respectively, of unknown causes—but not, it is stated, of lung trouble; an aunt died of consumption.

A year ago, at the climacteric, she began to suffer with shortness of breath, and puffiness of the face and neck for the past six months, and with occasional slight cough. From time to time she would have intense attacks of dyspnoea and orthopnoea, particularly upon slight exertion. At no time did she have any fever or any severe pain in the chest. Her appetite has always been poor, and for some time she has had slight difficulty in swallowing. The bowels were at first constipated, but now are regular. She has been under medical treatment throughout the year of her illness. The diagnosis at first was nervousness dependent upon the change of life; more recently she has been treated for emphysema of the lungs.

Upon examination I found her to be a large, fairly well-nourished woman, with cyanosis and puffiness of the face. She was sitting up in bed and breathing rapidly and with great difficulty. The openings of the sebaceous ducts all over the face were unusually large, the lips blue, the sclera dark and cyanotic. The neck was greatly enlarged, and all the natural depressions, particularly those above the clavicles, were obliterated. The chest was crossed by large veins, especially on the right side, above and below the breast. Resonance was impaired on the right side from the clavicle down to the liver, dullness and resistance being more marked above than below, and extending over beyond the right border of the sternum. There was some tenderness on percussion near the apex of the lung. Posteriorly there was dullness, but not flatness, at the right base, and some tenderness on percussion. Tactile fremitus was almost absent at that point. Auscultation revealed inspiration and expiration equal in length, but harsher over the right side in front than over the left. Posteriorly breathing was quite

distinct over both lungs, inspiration being a little harsher on the right side than on the left, and expiration having just below the scapula a distinct bronchial quality. Vocal resonance was well marked over the right side, and had a slightly twangy character. The heart did not seem to be enlarged; the apex-beat was not palpable, and there was no murmur. The temperature was 97.8°; the pulse, 108. There was a small amount of clear, tenacious sputum, which did not contain any tubercle bacilli.

The existence of the impaired resonance, diminished tactile fremitus, distant bronchial breathing, and twangy vocal resonance led me to suspect the presence of fluid, and on my second visit I made an exploratory puncture and withdrew a syringeful of clear serum. On the following day, November 11th, at noon, I tapped in the seventh interspace, postaxillary line, and, by means of the aspirator, drew off three pints of a somewhat turbid, yellowish fluid, frothing readily. After a little less than a quart had been removed the patient began to cough. At first the cough was dry, but toward the end of the tapping a little frothy fluid was brought up. The patient seemed to be dyspnoic and became blue in the face, and, as the cough grew more intense, I suspended the tapping and administered a small dose of morphine. As she did not seem to grow any worse under observation, I left her at 12.30, and saw her again at 6. During this interval she had expectorated about five ounces (160 c.c.) of a turbid, amber-colored fluid, covered with a layer of froth half as thick as the fluid itself, containing a few streaks of blood and some flocculi. The cough had not diminished to any great degree, but the expectoration had gradually lessened. The patient was very much more comfortable than she had been at noon, and decidedly better than before the tapping. Her temperature was 99.1° F.; respirations, 44; pulse, 108. On auscultation, moist râles could be detected over the anterior right lung from top to bottom, and there was the most exquisite crepitation on inspiration that I had ever heard. Pneumothorax was not present. On the following day there was still a little cough, but the patient was much better than she had been for a long time. The difficulty in swallowing had disappeared and there was good resonance over the right lung.

Unfortunately, the chest filled up again, and I had to aspirate a second time on November 24th, this time drawing off about a quart of fluid. There was again intense cough and a little tenacious sputum, but no true albuminous expectoration. At the last examination (made to day) I found the chest again full to the top. The dullness behind the sternum has increased in intensity and in extent, reaching now about two inches beyond the left sternal border, and fusing on the right side with the dullness of the fluid. A large, hard gland has also appeared above the left clavicle. The signs are sufficient to warrant a diagnosis of *tumor of the anterior mediastinum*, probably sarcoma, which is encroaching upon the right lung and compressing the veins that return the blood from the right pleural cavity.<sup>1</sup>

<sup>1</sup> The chest was aspirated for the third time on December 6, 1901, and more than three pints of fluid were withdrawn. A severe spasmodic cough ensued, but no albuminous expectoration. On December 19th the patient died of exhaustion, and at the autopsy a large sarcoma of the anterior mediastinum was found.

The aspirated fluid was of a turbid amber color and frothy. It coagulated upon standing, the clot floating at some distance from the bottom. The circumambient fluid was clear, straw-colored, and not gelatinous. It coagulated into a moist, solid mass on boiling, had a specific gravity of 1021, was faintly alkaline in reaction, gave the biuret test, was free from sugar, and did not form a precipitate with acetic acid. The amount of albumin present with Esbach's albuminometer was  $4\frac{1}{2}$  per cent. The total solids obtained by evaporating, thoroughly drying in the water oven, and standing for twenty-four hours in a desiccator, was 6.8 per cent.

The *expectorated fluid* was of a turbid amber color, was covered with a layer of froth to the amount of about half the thickness of the fluid, and had a thin sediment of blood. It was gelatinous, like the white of an egg, and coagulated upon boiling into a solid mass. The specific gravity was 1018; the reaction, neutral; the biuret test, positive. There was no sugar. Chlorides were present, and acetic acid produced a distinct precipitate. The albumin amounted to 3.5 grammes with Esbach's albuminometer; the total solids were 5.84 per cent.

As the terms albuminous, albuminoid, and sero-albuminous imply, the expectoration consists of a richly albuminous fluid. It is viscid, frothy, neutral, or faintly alkaline, and of a yellowish color; contains a little blood, and is coagulated upon boiling and by nitric acid. As a rule, it closely resembles in appearance the chest fluid. Acetic acid, as in my own case, usually gives a precipitate suggesting the presence of mucin. Urea, hæmoglobin, and the salts characteristic of serum are present; urobilin has also been found.

The expectoration seldom sets in during the paracentesis, but generally after an interval of from a few minutes to half an hour. In rare instances the interval has been prolonged to two hours, and in the case reported by Pepper it was apparently eighteen hours. During the interval the patient generally enjoys a marked feeling of comfort, which is suddenly terminated by dyspnoea and cough. Sometimes the latter begins before the tapping is finished. The cough rapidly becomes more intense and expectoration increases, the patient experiencing at the same time a terrible sense of oppression, which compels him to sit up in bed. The breathing is greatly labored; the face deeply cyanosed and very anxious; the skin clammy, the pulse rapid and weak. Auscultation reveals the characteristic coarse and fine moist râles of œdema.

In mild cases the symptoms subside gradually, the expectoration ceasing after several hours, sometimes, however, not until a day has elapsed. In extreme cases the fluid gushes from the mouth and nose in a constant frothy stream, the patient suffering the most

agonizing dyspnoea and not infrequently dying of asphyxia—drowned, as it were, in his own juices. The amount expectorated varies with the duration and the intensity of the attack; not rarely as much as a pint or even a quart is brought up in the course of one or two hours. Gee's patient expectorated a litre in two hours; Schütz's a total quantity of 1500 c.c.

The duration of the attack is, as a rule, from one to two hours, but in some cases it has been six, twelve, twenty-four, and even forty-eight hours.

On standing the fluid generally separates into three layers: the upper, whitish and frothy; the middle, opalescent and yellowish; the lower, denser and more viscid, and containing a few whitish flocculi. In my own case there were but two layers on standing: an upper, frothy layer, and a lower stratum, double the thickness, of opalescent fluid.

*Analyses of the Fluid.* I have already detailed the analysis in my own case. For purposes of comparison, I give below the few analyses of the pleural and the expectorated fluid that I was able to find in the literature. Many are incomplete.

1. Terrillon's Case. The pleural fluid contained 1.61 per cent. of albumin; the expectoration, 1.42 per cent.

2. Foucart states that the total solids in the pleural fluid were 7.5 grammes per litre; in the expectoration they were 100.3, the albumin being 93.6 and the mineral salts 6.7.

3. Daremberg and Dujardin-Beaumetz. *a. Pleural Fluid.* Specific gravity, 1020; albumin, 66.88 grammes per litre; urea, 0.58 gramme per litre; hæmatoidin crystals, biliverdin, and a notable quantity of mucosin.

*b. Expectorations.* Specific gravity, 1010; albumin, 1 gramme per litre; urea, 2.36 grammes per litre; cholesterin and fat.

4. Drivou. *a. Pleural Fluid.* 945.28 parts water, 54.72 parts solids. Of the solids, there were albuminoids 48.28, divided as follows: albumin, 25.69; hydropsin, 22.59; mucosin, a trace; salts, 6.44 per cent.

*b. Expectorations.* 976.86 parts water; 23.14 parts solids. Of the solids, there were 15.87 parts organic and 7.28 parts salts.

5. Laboulbène. *a. Pleural Fluid.* Specific gravity, 1020; total solids, 65 grammes per kilogramme. Of this, 6.078 were fibrin, 7.5 mineral matter.

*b. Expectoration.* The dry residue varied from 16.47 to 24.60 on different days; the mineral matter, from 3.53 to 7.8. The albumin was not estimated in the expectoration.

6. Besnier merely states that the quantity of albumin in the expectoration was double that in the effusion.

The analyses, it is seen, show enormous variations among themselves. In some cases the two fluids differed widely, in others they resembled each other very closely in composition. With regard to hydropsin, which, according to Drivon, is a substance characteristic of serous membrane exudates, I was unable to find any reliable data. Its existence is not recognized by physiological chemists of the present day.

Albuminous expectoration occurs especially after tapping in cases of acute effusion, although in my own case the effusion was unquestionably chronic. It has taken place with both left-sided and right-sided exudates and transudates. Of 32 cases, the effusion was left-sided in 18, bilateral in 4.

An important point, to which reference will again be made, is that in the majority of instances the amount of fluid withdrawn was inordinately large, and usually, but not invariably, the withdrawal was rapid. In some instances the simple trocar was used, in others the aspirator. Thus, there were withdrawn in the case of Woillez 5500 c.c.; in that of Marrotte, 5000; in Lande's two cases, 3000 and 1800 c.c. respectively; in Pinault's, 3000; in one of Besnier's, 2600; in Pepper's, 2400. Prévost tapped several times in the same case. At the first tapping he withdrew 1000 c.c., and there was no albuminous expectoration; at the second 3000 c.c. were withdrawn, and the expectoration followed. Subsequent punctures were not followed by any complication. In Schütz's case 2000 c.c. were removed.

In the majority of cases complicating conditions of various kinds existed and probably played a part in the production of the phenomenon. Lande believes that the danger of albuminous expectoration is particularly to be feared when the conditions on the opposite side are such as to lessen the play of the other lung. At *autopsy* the principal change is an oedema of the lung on the affected side—sometimes of both lungs. In cases in which the pleural effusion was of the nature of hydrothorax heart disease was found. Scriba's case is of interest because at the autopsy a fibrinous coagulum was dis-



covered plugging the bronchi. In the case of Hayem and Tissier there was adherent pericardium.

Various theories have been advanced in explanation of the curious phenomenon of albuminous expectoration. Terrillon divides them into four classes :

1. Perforation of the lung by the trocar.
2. Spontaneous rupture of the lung.
3. Absorption by the lung of fluid remaining after the tapping.
4. Pulmonary congestion, with intense œdema.

The first three assume that the fluid expectorated is a portion of the pleural exudate ; the last, that it is a transudate from the blood-vessels of the lung.

1. *Perforation of the Lung.* The identity in appearance of the two fluids and the analogy in composition—which latter, however, is not constant—suggest this view, which was first propounded by Woillez and Marrotte, and was held by Scriba and others. I may also say that when I examined and compared the two fluids in my own case I was at first inclined to this theory, but against such an interpretation are the following weighty arguments :

1. The absence of pneumothorax, which should be present if the lung had been punctured by the trocar.

2. The late onset of the expectoration. If connected with perforation of the lung it ought to set in at once, and not after an interval of half an hour or more from the time of tapping.

3. The absence of hæmoptysis.

4. The fact that albuminous expectoration has occurred especially in cases in which the effusion was very large and the lung, of necessity, far away from the chest wall.

5. The large amount of expectoration. It is hardly conceivable that a pint or a quart of fluid could, in a short space of time, pass through such a small opening as would be made by the point of a trocar.

6. In some instances the expectoration occurred several times in the same case. Thus the patient whom Behier tapped four times had albuminous expectoration each time, and in the patient of Gee every one of the three tapplings was followed by albuminous expectoration. It is unlikely that the lung in these cases was punctured so many times. Moreover, both writers state that, warned by their first experience, they afterward tapped with the greatest care, so as to avoid wounding the lung.

7. In none of the fatal cases was any perforation of the lung found post-mortem. This, to be sure, is not an argument of great force, for it is proverbially difficult to discover perforations in cases of pneumothorax and of empyema rupturing into the lung: but, on the other hand, the argument is not to be held too lightly, since, death being so much more prompt in albuminous expectoration than in pneumothorax or empyema, the chances of finding a perforation should be better.

II. *Spontaneous perforation of the lung* is the view defended particularly by Féréal. The excessive rarity of serous effusion perforating into the lung is against this. Furthermore, there is no reason why it should occur just at the end of tapping: and this, together with the non-development of pneumothorax, the failure to find the perforation at autopsy, and the absence of the auscultatory signs of pleurobronchial fistula, is sufficient to dispose of this theory.

III. *Absorption of Fluid by the Lung.* This is an illogical view, for it must at once be apparent that the absorption or sucking up of the fluid through the stomata of the lung would cause it to enter the lymphatic system, and not the bronchi.

IV. *Pulmonary Edema.* This theory was first advanced by Pinault, and was strongly advocated by Behier. It is the one adopted by Pepper, West, and most recent writers. In support of it we have the following arguments:

1. The onset of the expectoration a little while after the tapping is completed.

2. The physical signs of oedema—crepitant and subcrepitant râles—are present.

3. Edema of the lungs was the chief lesion found in those organs at autopsy.

4. The occasional development of albuminous expectoration in the absence of pleural effusion. Thus, Foucart reports a case in which it occurred in a patient with heart disease without pleurisy, and Woillez observed it twice in emphysematous asthma and once in aneurism of the aorta. In his cases the expectoration did not contain any mucin.

5. The occurrence of the phenomenon after tapping in empyema, as in the case of Fraser. The rarity of albuminous expectoration after the evacuation of a pyothorax has been well explained by

Curtin, who ascribes it to the fact that, owing to the thickness of the fluid, the abstraction is necessarily slow.

6. The chemical composition of the two fluids tells both for and against the œdema theory, inasmuch as the fluids sometimes differ and sometimes appear to be almost identical; but, as it is not possible to discover any clinical difference between the two groups of cases, it is fair to assume that, even when the expectorated fluid most closely resembles that from the pleura, its origin is the same as when it differs the most widely.

7. In the majority of cases in which albuminous expectoration occurred, the amount withdrawn was excessively large: in many instances, but not in all, the withdrawal was also rapid.

8. As stated by West, theoretical grounds are in favor of this view. The compressed lung is suddenly released from pressure, and there is naturally a great afflux of blood. A congestion follows, for which I should like to propose the name of *congestion by recoil*. It is true an increase of pressure in the pulmonary circulation is not alone sufficient to produce œdema: but we have in the condition here considered more than mere pressure—we have vessels that, by reason of their long compression and the altered circulatory conditions, have suffered a change in their walls, on account of which, we may strongly presume, they are rendered more permeable. A transudation occurs into the air vesicles which finds its way into the bronchi and is expectorated. It is possible that the negative pressure exerted upon the heart by the expanding lung, intensifying the diastolic relaxation of the organ, and thus embarrassing its action, is a factor in the production of the phenomenon. The negative-pressure effect was first adduced by Dr. Mary Putnam-Jacobi in explanation of the sudden syncope sometimes following thoracocentesis. Lande was of the opinion that the œdema was due to the irritation of the air rushing into the expanding lung, while Johnson believed that it was favored by the existence of thrombosis in the vessels, the result of the long-continued compression and stagnation of the blood. This, however, is not tenable, because such a thrombosis would produce infarction; and of the existence of this there is no evidence in cases of albuminous expectoration. Duffin's view of a vasomotor paralysis of the vessels, in consequence of the prolonged compression, is not unreasonable, and

helps to account for the congestion : but whether there be a vasomotor paralysis or a nutritional change in the vessel walls, there is, in either case, a relaxation and a sudden afflux of blood to the expanding lung. The subsequent event—the transudation of serum—is best explained on the assumption of an alteration in the walls of the capillaries and small vessels themselves, such as Cohnheim has assumed follows prolonged compression.

**TREATMENT.** The cough is usually so intense that, despite the apparent contraindication of the drug, morphine cannot be dispensed with, at least in the severer cases. It is advantageously combined with atropine. Counter-irritation, in the form of mustard or dry cups, should also prove of value. Artificial respiration and venesection suggest themselves as theoretically beneficial. The former has had a practical trial in one case without avail; the latter, so far as I have been able to determine, has not been employed.

**CONCLUSIONS.** 1. Albuminous expectoration is a very rare complication of thoracocentesis. It is usually serious, and sometimes fatal.

2. It consists in the expectoration of a viscid albuminous fluid closely resembling the fluid of serous effusion.

3. The condition is best explained on the basis of an intense congestion and oedema of the lungs (congestion by recoil).

4. The principal cause seems to be either too rapid or too great a withdrawal of fluid.

5. Serious cardiac disease and morbid conditions of the opposite lung, hindering expansion, are predisposing causes.

6. Under all circumstances, but particularly when these complications exist, aspiration should be performed slowly. If the effusion is large, the amount withdrawn at any one time should be moderate.

7. In some cases it may be wise to perform several tapplings, drawing off a small quantity each time.

8. The treatment consists of counter-irritation, venesection, and artificial respiration, together with the use of morphine if the cough is severe.

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REPORT OF SEVENTY CASES OF HEAT FEVER,  
ONE OF HEAT MENINGITIS, AND THIRTY-  
FIVE OF HEAT EXHAUSTION  
IN MALES.

TREATED AT THE PENNSYLVANIA HOSPITAL IN 1892.

PRECEDED BY AN HISTORICAL AND STATISTICAL REVIEW OF THE  
STUDY AND TREATMENT OF THE PATHOLOGICAL EFFECTS  
OF ATMOSPHERIC HEAT BY THE STAFF OF THE PENN-  
SYLVANIA HOSPITAL FROM ITS FOUNDING,  
1751, TO THE PRESENT DAY, 1901.

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[Read June 1, 1901.]

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ABSTRACT.<sup>1</sup>

THE courtesy of Dr. Richard Wilson contributes the reports of 9 cases of women treated for the effects of atmospheric heat in 1892 at the Pennsylvania Hospital, to the 27 cases of men cared for in the same institution during the same summer, and now reported. This combined report of 106 cases—70 of heat fever, 1 of heat meningitis, and 35 of heat exhaustion—is made with the kind permission of Dr. Morris J. Lewis and of Dr. Arthur V. Meigs, in whose services the cases occurred. The latter can be viewed in more just proportion if their consideration is preceded by a review of the study and treatment of the pathological effects of atmospheric heat by the staff of the Pennsylvania Hospital from its founding, 1751, one hundred and fifty years ago, to the present day.

<sup>1</sup> The length and detail of this paper render it unsuitable for publication in full in the *TRANSACTIONS*. It will later receive such publication, with more complete statistical analysis and with illustration.

## HISTORICAL REVIEW, 1751-1901.

Biblical references<sup>1</sup> to fatality following exposure to the sun are followed after the lapse of centuries by the observations of Forestus<sup>2</sup> in 1562, of Baglivi in 1694, and of Lancisi in 1705.<sup>3</sup> These three observers confounded the effects of heat with the symptoms of apoplexy, and this confusion was perpetuated by some observers<sup>4</sup> up to 1852. Forestus was the first to distinguish two types of cases, the mild and the fatal. Baglivi and Lancisi also recognized the predisposing influences of heat and humidity, and added that the depressing influences of prevalent war were contributory.

In 1769, eighteen years after the founding of the Pennsylvania Hospital, its records show the first entry of the pathological effects of heat—under the diagnosis of “hurt by drinking cold water.” Fifteen similar entries, making a total of 16 cases and of 3 deaths, are entered on the Hospital Register prior to 1831, when the phrase *coup de soleil* appears for the first time, showing an advance in the etiological appreciation of these cases. The last entry of “drinking cold water” is made on June 10, 1838.

In 1811 Hillary's work on *Tropical Diseases*, with notes by Benjamin Rush, states that apoplexies (evidently cases suffering from heat) occur frequently in Barbadoes in July. This is the first published communication upon the bodily effects of heat from a member of the staff of the Pennsylvania Hospital.

In 1814 Dr. Coates, as he reported in 1858 in his discussion of Dr. Levick's paper before this College, “Inhabited the Pennsylvania Hospital.” He recalled that at this time, by order of the Humane Society, the public pumps were posted with cautions against sudden death from drinking cold water. He saw many persons at the Hospital (Pennsylvania) alleged to be suffering from a spasmodic affection of the stomach, described by Dr. Rush as a result of drinking cold water; but it was Dr. Coates' opinion and that of some medical attendants at the hospital that these patients

<sup>1</sup> J. J. Levick. American Journal of the Medical Sciences, 1859. xxxvii. 40.

<sup>2</sup> Loc. cit., p. 49.

<sup>3</sup> Loc. cit., p. 48.

<sup>4</sup> C. H. Gordon. Medical Times and Gazette, 1857.



were usually under the influence of ardent spirits and suffered rather from congestion of the brain than that of the stomach. Among other remedies mentioned by Dr. Coates is the application of cold to the head. This is the earliest mention found of the use of this agency in these cases. He comments that the great terror of the destructive effects of the use of ice in drinks, etc., and its apparent dangers were then (1858) forgotten.

In 1830 Gerhard<sup>1</sup> (article on "Apoplexy") observed similar post-mortem appearances in a man who died with cerebral symptoms during the hot weather that year, but who did not have apoplexy, and also in twenty or thirty persons whom he had seen opened subsequent to death from heat. He observed in all but slight congestion of the brain.

In 1834 the first report of congestion of the lung as a post-mortem observation in the cases of three soldiers, was made by J. J. Russell, of the 73d Regiment, English Army.

In 1845 Dr. Dowler makes the first American differentiation of the effects of heat as: "1. Solar exhaustion or syncope. 2. Solar or sun pain. 3. Solar excitement or inflammation. 4. Solar asphyxia." He says "solar asphyxia" is always fatal. In other words, heat exhaustion, meningitis, fever, and an extreme and rapidly fatal degree of the latter. He also reports the first observations of such bodily temperatures as 111°, 112°, and 113° F., and reports from his own observation, post-mortem, congestion of the lung.

In 1849 Dr. Henry Hartshorne was the first of the staff of the Pennsylvania Hospital (he being a resident physician) to publish a report<sup>2</sup> of *coup de soleil*. He described four cases treated in 1848; two were fatal. He also makes the first mention found of the application of ice to the head in the treatment of these cases.

In 1850<sup>3</sup> Dr. William Pepper, the elder, reported before this College 20 cases treated at the Pennsylvania Hospital in the seven preceding years. Of these, 10 died, 7 recovered, and 3, partially recovered, became insane. All of these cases had been bled before admission to the hospital. Dr. Pepper reports symptoms and post-mortem appear-

<sup>1</sup> Graves and Gerhard. System of Clinical Medicine. Philadelphia, 1848

<sup>2</sup> American Journal of the Medical Sciences, 1849, N. S., xviii. 66.

<sup>3</sup> Ibid., 1851, p. 183.

ances. Both these conditions were possibly modified by the bleeding to which the patients were subjected before being admitted to the hospital. Dr. Pepper says: "The disease is evidently one of nervous exhaustion. The cases of apoplexy and congestion of the brain occasionally produced by insolation should be carefully distinguished from the cases above alluded to, the pathology and treatment of the two being very different." Again: "The cases we usually meet with during the intense heat of our summers present no symptoms similar to those which result from cerebral congestion, and demand for their cure stimulants instead of bleeding." Dr. Pepper closes by commenting on the absence of satisfactory medical literature on the subject at that day. This was the first presentation of this topic to this college, and it is, also, the first, though not a very clear, recognition by a member of the staff of the Pennsylvania Hospital and by a Fellow of this College of the difference between exhaustion and congestion following exposure to the sun.

Dr. Condie, in discussion of Dr. Pepper's remarks, gives a most clear and differential description of the symptoms of exhaustion from heat, and also (which Dr. Pepper did not) of congestion (fever) from heat. He also makes distinction in the treatment, condemns bleeding for heat exhaustion, and, on the other hand, tells how he saved life by bleeding in a case of heat congestion accompanied by convulsions. He also shows his recognition that artificial heat as well as solar heat can produce the phenomena at that time generally only attributed to the sun.

In 1852 Gordon,<sup>1</sup> an English Army officer, states that apoplexy and *coup de soleil* include the same conditions of body. His paper is important as bridging the epochs in one of which the effects of heat were ill described as apoplexy, while in the other the terms insolation and sunstroke evinced a correct appreciation of the exciting cause in some cases, although both terms are too restricted in meaning to embrace the bodily effects of artificial as well as of solar heat. He bled his patients, and gives the first report found of treating these cases with cold affusions.

In 1853 Dr. T. H. Bache, resident physician of the Pennsylvania

<sup>1</sup> Medical Times and Gazette, 1857.

Hospital, as he reports in a discussion of Dr. Levick's paper read before this College in 1858, attended a number of sunstroke cases—they were mostly fatal (6 out of 10 cases)—and the post-mortem condition of the heart was not softened, as reported by Pepper of the cases he had seen.

In 1857 Dr. B. Darrach, resident physician in the New York Hospital, treated 4 cases by stimulants and by rubbing the entire surface of the body with ice: 3 of his cases recovered, 1 died. He reports the cases equal in severity to 4 previous cases in which the ice was only applied to the head, and all 4 patients died. This is the first report of the application of ice to the whole body in the treatment of this condition.

In 1858 Dr. Levick<sup>1</sup> reported to this College 12 cases treated that year at the hospital: 1 of these cases occurred in a sugar refinery, 3 cases died, and also a cured case suddenly on the sixth day after recovery. Dr. Levick emphasized the differences between exhaustion and congestion as bodily results of heat, and urged that for these dissimilar conditions different modes of treatment were required, and that therefore diagnosis was important.

In January, 1859, Dr. Levick contributed to the *American Journal of the Medical Sciences* a comprehensive history of this subject, to which this review is much indebted. He alludes to some cases with symptoms similar to those exhibited in *coup de soleil*, reported by Dr. H. H. Swift,<sup>2</sup> as occurring in a laundry, and to a case reported by himself a year before, and which had developed in a sugar refinery. This allusion is to bear out the statement that solar heat is not the only cause that produces the group of symptoms described—that is, they also arise from artificial heat. Commenting upon terminology, he says: "The term sunstroke or heatstroke, so long as we remain uncertain as to the exact pathological condition, may as well be retained." The term heatstroke, here found recorded for the first time, is an advance in terminology, because applicable to cases suffering from the effects of artificial as well as of solar heat.

In 1863 Dr. Horatio Wood, Jr., published in the *American*

<sup>1</sup> TRANSACTIONS OF THE COLLEGE OF PHYSICIANS, 1858.

<sup>2</sup> New York Journal of Medicine, 1854, N. S., vol. xli. p. 45.

*Journal of the Medical Sciences* a report of 8 cases affected by heat, 7 of which died: a ninth case that died is recorded in the hospital records, and was probably not under Dr. Wood's care. He expresses his belief that heat produced different classes of cases called sunstroke, but he had observed only the fatal variety he had reported. The maximum temperature observed during life was  $109\frac{1}{4}^{\circ}$ , but one hour after death the temperature of  $110\frac{3}{4}^{\circ}$  was recorded in one case. The blood was usually dark and fluid and the heart invariably contracted. He states that alterations in the blood produced by heat are responsible for the cerebral symptoms observed, that death is brought on by loss of power in the central nervous system, and he substitutes "thermic fever" as the name of the condition in place of sunstroke. The name thermic fever is an advance in specific terminology, because the first word accurately gives the cause of the trouble, and the latter word states the condition resulting from the cause: the two words combined limit their application to the grave form of bodily effects from heat which is accompanied by an elevation of temperature that tends to the extreme. He condemns the prejudice against drinking water, and urges the ingestion of fluids, because the blood has been deprived of its serum, it may be by pints, through the action of the perspiratory glands. He acknowledges treatment to have been futile in his hands, and quotes and suggests Taylor's<sup>1</sup> recommendation of cold affusions as practised in India.

In 1866 Dr. George B. Wood, in the sixth edition of his *Practice of Medicine*, advocates the term heat fever in preference to the term thermic fever, suggested by Dr. Horatio Wood, Jr. Either of these names he prefers to insolation, etc., because the condition in mind is a consequence of heat, but not exclusively of solar heat.

In this same year Dr. Levick (as he reports in 1868) treated 22 cases in one week at the hospital. Of 12 cases treated by affusions and entire bath 7 died. Of 7 rubbed with ice, 6 recovered: 2 of these cases had temperatures of  $109^{\circ}$ . This is the first record of recovery from such a temperature.

In 1868 Dr. Levick, in his first volume of the *Pennsylvania Hospital Reports*, contributes a paper entitled "Heat Fever," and

<sup>1</sup> Lancet, 1858.

credits the title to Dr. George B. Wood. He recognizes three dissimilar conditions resulting from exposure to heat: 1. A condition of loss of power (exhaustion). 2. Meningitis. 3. Heat fever. Dowler had made this same classification with a different terminology. Dr. Levick reports in his paper the microscopical examination of the blood of a fatal case and the observation of crenated corpuscles. He also refers to the experimental production of the symptoms of heat fever in animals by Dr. R. Cresson Stiles, reported in the *Boston Medical Journal* of June, 1864. This is the first microscopical and experimental work on this subject that has been found.

In 1868, in the second volume of the *Hospital Reports*, Dr. James Hutchinson publishes a paper upon the success of one-fourth-grain, hypodermic doses, of morphine in the control of convulsions in 4 cases<sup>1</sup> of sunstroke treated at the hospital that year. The injections were given by Dr. Herbert Norris, resident physician.

In 1872 Dr. Horatio Wood, Jr., was awarded the Boylston Prize for his "Dissertation on Sunstroke." Dowler's and Levick's triple classification of exhaustion, meningitis, and fever is repeated. The essayist, however, adds that the classification of meningitis is theoretical, and that his experience had brought to his observation but a single case that might be classed as that of exhaustion. This treatise devoted itself to the history, and more especially to the pathology, of this subject. It reports negative examinations of the microscopical appearances of the blood, in contrast to the observations of Levick. It presented much original experimental work, the possibilities of treatment, and a consideration of the sequelæ. It was not only the most scientific and exhaustive presentation of this subject at that day (1872), but it still remains so.

From this elaborate study Dr. Wood was convinced that "the nature of sunstroke is that of a fever, or, in other words, that *coup de soleil* is a fever not dependent upon blood-poisoning, but upon heat, an ephemeral or irritative fever, if the term be preferred."

Further on, he says that when a man is exposed to heat beyond his powers of resistance there is a gradual slow rise of temperature until the stimulus of the heat becomes so intense as to paralyze either the

<sup>1</sup> Dr. Hutchinson's report only mentions 4 cases in which morphine was given hypodermically, and not 16, as stated on p. 110 by Dr. Horatio Wood, Jr., in his "Prize Essay."

heat centre or the vasomotor nerves, as the case may be, and then there is a sudden intensifying of the oxidation process, and a further rise in temperature, preceded, accompanied, or followed by an overwhelming of the cerebrum; in other words, intense fever, with its accompaniments, is developed. In the chapter on Treatment it is of interest to note that McClean used and advocated chloroform anæsthesia for the control of the convulsions.

In 1885 the hospital registers and the bound volumes of the medical histories written by the resident physicians show that there were treated at the hospital of that year 15 cases of heat fever and 16 cases of heat exhaustion, 31 cases in all. Nineteen cases must have escaped the hospital record, for Dr. Horwitz (one of the resident physicians at the hospital in that year) wrote a report, communicated to this College by Dr. Jacob Da Costa, and entitled "Observations on Sunstroke and Heat Exhaustion, Based on the Record of Fifty Cases Admitted into the Pennsylvania Hospital from the Month of July to the Middle of August, 1885." The employment of antipyrin in rectal injections and the etherization and treatment with rectal injections of musk in cases suffering from convulsions are interesting features of this report. Dr. Horatio C. Wood and Dr. Da Costa concurred in the discussion that this use of musk and antipyrin was original with Dr. Horwitz, and that subsequent to this use in July of antipyrin by Dr. Horwitz, there was published in August by a resident physician of the New York Hospital a similar use of the drug. Dr. Horwitz also has the distinction of recording the first recovery achieved in a case reaching the temperature of 112°.

In 1887 the hospital received and treated the greatest number of cases (44) occurring in one year, and suffering from heat, that it had recorded up to that time. Thirty-three of these cases had heat fever and 11 heat exhaustion.

In 1888 Dr. Frederick A. Packard, resident physician, reported in the *American Journal of the Medical Sciences*<sup>1</sup> "Thirty-one Cases of Heat Fever Treated at the Pennsylvania Hospital During the Summer of 1887." This report is the most elaborate and systematic,

<sup>1</sup> Vol. xcv., N. S., p. 554.

in its presentation of the symptoms observed and the treatment employed, yet presented. The cases are not only reported in abstract, but the symptoms and treatment are most conveniently tabulated.

The reduction of temperature was accomplished in cases above 106.4° F. by surrounding and rubbing the patient with ice; cases below 106.4° F. were sponged with alcohol and iced water. Obstruction to capillary and venous circulation was met by bleeding, and convulsions by morphine.

In 1892 the hospital received and treated 106 cases suffering from heat, the greatest number received in any year by the institution from its founding to the present day, June, 1901—one hundred and fifty years. Seventy of these cases suffered from heat fever, 1 from heat meningitis, and 35 from heat exhaustion. The novel elements in treatment used at this time, and at the instance of Dr. Morris J. Lewis, were devoted to the prevention and dissipation of capillary and venous stasis—*i. e.*, of cyanosis by the use of forcible spraying and rough friction with loofah sponges; also to the reduction of temperature and the favoring of increased blood fluidity by iced enteroclysis.

Dr. W. M. L. Coplin in this same year of 1892 reported "The Effects of Heat as Manifested in Workmen in Sugar Refineries."<sup>1</sup> The number of cases treated was 213—heat fever, 193; heat exhaustion, 20. The fact that the cases were produced by voluntary exposure to artificial heat, increased by an exacerbation in the atmospheric heat, and that on the occurrence of abnormal symptoms their subjects were immediately placed under medical observation and treatment, almost places the report under the category of an experimental inquiry. The treatment was carried out in the refinery with exceptionally good equipment, and comprised some novel elements. Some of these were coincident, though of independent origination, with those employed at the hospital in this same year—namely, forcible spraying and rough friction in the treatment of the capillary and venous stasis manifested as cyanosis. The use of nitrite of amyl, in a single case and with favorable result, in control of convulsions and improvement of the peripheral circulation, is

<sup>1</sup> Medical News, 1892, lxi, 262.



the first recorded. The amenability to treatment of the effects of extreme heat, when immediate and proper measures are instituted, as illustrated by this report, is in contrast to the terrible mortality under other circumstances. The promptness with which the aid could be rendered permitted but two cases to reach a temperature above  $108^{\circ}$ . Both of these cases were taken to the hospital: the temperature of one was  $108.8$ , and it recovered; that of the other was  $110^{\circ}$ —it resisted for hours the treatment afforded it at the refinery, and died one and three-quarter hours after it was admitted to the hospital. This was the only fatal case of the 213 reported.

In 1896 Dr. Frederick A. Packard, in the *American Text-book of Applied Therapeutics*, makes the first suggestion of a remedial measure that promises to be second in importance only to the use of ice in combating the effects of heat. In a most comprehensive and able chapter upon "Diseases Dependent upon External Heat," he says (p. 1132): "A measure that seems to me theoretically to offer some possibilities is hypodermoclysis. The thick, tarry condition of the blood obtained by venesection points strongly to the possibility of decreased serosity being at least one factor in the complicated condition produced by excessive heat. The method seems to me certainly worthy of trial."

In the same year, in the *Medical News*,<sup>1</sup> Dr. Packard reports the beneficent influence of hypodermoclysis (normal salt solution, one-half pint) employed at the hospital on August 12, 1896, in a case that had reached a temperature of  $109.6^{\circ}$ , and that had been convulsed and cyanosed. It is of interest to note that this case had been bled (flxxvi), and that it had received hypodermically  $\frac{1}{100}$  of nitroglycerin, the first record found of the use of this well-indicated drug in this condition.

This is the most recent contribution to the literature on this subject from a member of the staff of the Pennsylvania Hospital. The total number of cases suffering from the effects of heat recorded in the hospital registers from 1751 to 1901 is approximately 926. Of this number 140 cases were fatal. A comparison of the percentages of mortality occurring in the years when more than 10 cases with a

<sup>1</sup> Vol. lxxix, p. 213.

temperature above  $108^{\circ}$  were received, will be found on p. 291 of the report that follows this review. An analyzed, full, and tabulated account of the important and interesting influence of the staff of the Pennsylvania Hospital upon the history of the treatment of the effects of heat will receive later publication.

REPORT OF SEVENTY CASES OF HEAT FEVER, ONE OF HEAT  
MENINGITIS, THIRTY-FIVE OF HEAT EXHAUSTION; NINE  
FEMALES, NINETY-SEVEN MALES; TOTAL ONE  
HUNDRED AND SIX IN 1892.

The credit for correctly naming the gravest bodily effect of atmospheric heat, "thermic fever," belongs to Dr. Horatio Wood, Jr. Dr. George B. Wood translated this title into "heat fever." The latter term will be employed throughout this report. As a bodily temperature of  $100^{\circ}$  F. is accepted as that of fever, that standard is employed in the classification of the cases now reported.

GROUPING OF CASES. With one exception, the first day, all patients suffering from heat in 1892 were received in two periods, as may be seen in the following table:

Grouping of cases.	Date.	Max. temp. Fah.	Max. relative humidity.	Cases heat fever.	Cases heat meningitis.	Cases heat exhaustion.	Died.	Cured.	Total cases.
	1892								
2 cases, 1 day.	Friday July 15	93.0°	67	1	...	1	1	1	2
	July 23 Sunday,	90.0°	73	1	...	...	...	1	1
	July 24	82.5	81	3	...	2	...	5	5
	" 25	84.8	73	8	...	4	2	10	12
	" 26	84.4	68	5	...	2	...	7	7
1st group, 87 cases, 10 days.	" 27	85	69	9	1	2	2	10	12
	" 28	98.0	65	28	...	10	7	31	38
	" 29	99.0	85	3	...	5	1	7	8
	" 30	86.5	85	3	...	5	1	7	8
	Sunday, July 31	80.5	97	1	...	...	...	1	1
	Aug. 1	77.5	98	1	...	2	...	3	3
	Aug. 9	84.5	89	1	...	1	...	2	2
2d group, 17 cases, 3 days.	" 10	87.5	72	5	...	1	...	6	6
	" 11	94.0	72	4	...	5	1	8	9
Totals.	.....	.....	...	70	1	35	14	92	106

The greatest number of cases (38) and the greatest number of deaths (7) occurred not on the hottest day, July 26th, which had a temperature of 102° F., but on July 29th, temperature 99° F., the eighth consecutive day upon which the temperature had been 90° F. or above it. The inference follows that persistent rather than extraordinary heat is productive of bodily harm. The precise etiological value of humidity in the production of cases affected by heat is not apparent in this table.

The first day's work in treating physical conditions arising from heat suggested the possibility of over-treatment and the necessity of convenient tabulated treatment sheets. These were posted by dictation to a nurse, and this detail rendered the present report possible. Hurry and ignorance of the excellent tabulated report of Dr. Frederick A. Packard in 1888 prevented a fuller tabulation of symptoms.

*The time of day* at which the greatest number of heat fevers was received was from 11 o'clock till noon, and from 4 to 5 in the afternoon—that is, at the close of the two working periods of the day. This is strongly suggestive of the etiological influence of fatigue and exertion. The great mass of heat fevers and exhaustions was received between 10 A.M. and 5 P.M. The hour at which the greatest number of cases was received was that from 11 o'clock till noon.

*Sex.* Nine of the 106 patients treated for the effects of heat were women; of these, 5 suffered from heat fever and 4 from heat exhaustion. The remaining 97 cases were men, 65 having heat fever, 1 heat meningitis, and 31 heat exhaustion.

*The age* of more than two-thirds of the cases was between twenty and forty years; of more than one-half the cases from twenty to thirty years; of a little less than one-third of the cases thirty years, a period of exposure and activity. The extremes of age were from seven months to seventy years.

*Color.* Of the 106 cases, but 2 were of the colored race, and their complaint was that of exhaustion. This immunity is consistent with the statistics of this subject, and is rather to be expected from a tropical race.

*Nationality.* Of the 106 sufferers from heat the nationality of 49 cases was foreign; of 40 cases, American; in 17 instances it was unrecorded. Four-fifths of the cases of foreign birth were afflicted

with heat fever; three-fifths of the native cases suffered from heat exhaustion. Of any one nationality, the Americans represented about one-third of the total number of cases, and the Germans and Irish in the order named each represented about one-sixth, or together comprised one-third. Of the cases of heat fever (the total of which was 70), the Americans (14), the Irish (12), and the Germans (11) each contributed approximately the same proportions. These statistics are in confirmation of other observations that the unacclimated foreigner is not only especially predisposed to suffer from heat, but from the gravest form of malady resulting from it, heat fever.

*Occupation.* The heavy indoor occupations furnished about the same number of cases of heat fever as the heavy out-of-door labor. But the light indoor occupations were represented by about nine times as many cases of heat fever as the light out-of-door vocations. This possibly is because the latter are in smaller proportion. The indoor occupations as a total furnished about two-thirds of the cases of heat fever, the remaining third being made up of those employed out-of doors. The greatest number of heat-fever cases from one vocation was that of 8 sugar-house laborers: next in order came 7 out-of-door laborers and 6 teamsters.

*Alcohol.* Whether the abuse of alcohol predisposes to evil influences from heat will be investigated and reported subsequently. Of the 14 deaths, 2 occurred from delirium tremens several days sequent to immediate recovery from heat fever.

*Premonitory symptoms* occurred in a number of cases, and in several antedated the attacks by as long a period as twenty-four hours.

*The temperatures*—mostly rectal—observed on admission are tabulated below. The number of cases recorded under each degree of temperature includes all cases between that and the next higher degree of temperature.

## HEAT EXHAUSTION.

Temperature, Fah. . . . .	96°	97°	98°	99°	Unrecorded.
Number of cases . . . . .	1	2	3	24	5

## HEAT MENINGITIS.

Temperature, Fah. . . . .	100°
Number of cases . . . . .	1

## HEAT FEVER.

Temp. Fah.	100°	101°	102°	103°	104°	105°	106°	107°	108°	109°	110°	111°
No. of cases	21	4	6	5	4	1	2	3	6	7	9	2

Heat Stroke	Heat exhaustion . . . . .	35 cases.
	Heat meningitis . . . . .	1 case.
	Heat fever . . . . .	70 cases.
	Total . . . . .	106 cases.

The skin in the fever cases was dry and hot to the hand; in the exhaustions it was cool and moist.

A still greater number of high temperatures would have been recorded, but that the necessity for prompt treatment obliged that patients be iced on their way to the hospital, or when, on their admission, the clinical thermometer so suggested, be turned at once into an ice bath, without waiting for the registry of maximum temperatures.

*The pulse and respiratory rate* of the heat-fever cases generally increased with the temperature, and as the latter became very high decreased in strength. Groaning and stertorous respiration characterized marked cases.

*The physical characteristics* of the cases of heat fever, as a class, were those of large development and a tendency toward plethora.

*The cerebral condition* of pronounced cases of heat fever graded from stupor to unconsciousness to delirium. Head pain was a very frequent premonitory symptom and persisted late in convalescence. The large majority of the cases treated exhibited unconsciousness, which is frequently the initial symptom of attack in all three forms

of illness from heat. Unconsciousness is not exclusively a symptom of heat, and an examination of the head, the chest, the urine, and, if possible, the blood, considered in conjunction with the temperature, will help to minimize the tendency to see nothing but heat effects in every unconscious case in torrid weather. Apoplexy, alcoholic convulsions, and coincident malaria can perplexingly simulate heat effects, and the possibility of uremia must be borne in mind. In mild cases consciousness promptly returns on the application of cold to the head, and in some cases the patient, on becoming conscious, at once indignantly demands his clothes and liberty to return to work or home. The fear of fatal relapse, which has followed the granting of such requests, should refuse them, if possible. This class of cases is of that inconvenient degree of mental derangement that its constituents are too irrational to be permitted—and yet too sane to make it legally safe to deny them—their liberty.

*Convulsions.* There is record of 17 cases being convulsed. The convulsions were of tonic character and usually accompanied by rhythmical exacerbations that gave them a clonic appearance. They graded in degree from rhythmical twitchings of slight character, that were instantly aggravated by any peripheral irritation, to tonic convulsions with acute flexion of the forearms, vessels engorged apparently to the point of rupture, a countenance of alarming and deepening purple, and a violence that bespoke an instant and horrible death which did not occur. Complete opisthotonos was observed in some cases. In one instance the convulsion tended to approximate the head and the extremities of one side. Convulsions of local limitation were also observed as painful cramp in the muscles of the leg and agonizing cramp of the abdominal muscles. Patients that suffered so, gritted their teeth and clutched at their abdomen as though attempting evisceration. Contraction of the pupils was more often noted than the reverse.

*Cyanosis* was marked in the grave cases, and gave the skin a mottled appearance that called to mind some of the veined marbles or mottled soap.

*The urine* of 14 cases of heat fever and 1 of heat exhaustion was examined on the second or third day of convalescence, and six observations of albuminuria recorded. In some of these cases there was

sufficient in the patient's history to account for the albumin discovered independently of the recent illness from heat.

*The feces* were characterized by a pungent odor.

**TREATMENT.** The scheme of treatment pursued was mapped out, in anticipation, by Dr. Morris J. Lewis in the spring.

*Conveyance to hospital* of the cases was by ambulance, police patrol wagon, and a few cases walked in and requested relief. Treatment on the way was accorded on snap diagnosis largely made from the temperature of the skin as appreciated by the hand. Nearly all of the cases were unconscious; all were made recumbent. The exhaustions, if able to swallow, were given aromatic spirits of ammonia: if not, they received whiskey and strychnine hypodermically. Ice was carried in the ambulances and patrols; it was put at the head of the fever cases, the garments covering the trunk were thrown open, and the head and chest rubbed with ice.

It was in the original plan to give patients with high temperature hypodermic dosage of antipyrin guarded with brandy. In practice it was found too difficult for one person to sufficiently strip a patient in an ambulance to insert a thermometer in the rectum; and if the thermometer were placed in the axilla, it required such care as to prevent the more necessary remedial measure of rubbing with ice, and so the administration of antipyrin was prevented.

*The place of treatment* for the men was a cemented, high-fenced yard, covered by a double awning, artificially well lighted at night, supplied with water and a drain, and situated between the North House<sup>1</sup> and the low buildings near the entrance through the east or Eighth Street wall. The yard and awning were cooled by sprinkling with the hose; and, though this added moisture did not seem to work a disproportionate disadvantage by increasing the humidity, yet this possibility must be kept in mind. The women were cared for in an open but screened summer-house that stood between the end of the western wing of the main building and the western or Ninth Street wall.

The equipment consisted in iron cots with McIntosh encased

<sup>1</sup> Supplanted in 1895 by a new receiving ward and clinic building.



mattresses having a central opening for drainage and bowel movements; a portable tub; a hose with a rose spray; a large garden syringe with a coarse rose spray; an abundance of ice, and large pans; thermometers registering temperatures above  $110^{\circ}$ , and kept in carbolic solution, but dried before use; hypodermic syringes kept in carbolic solution; filtered and sterile hypodermic solutions; a supply of tabulated symptom and treatment sheets, and a nurse who kept them posted; a number of coarse loofah sponges and Turkish towels; a couple of Davidson rectal-bulb syringes.

*On admission*, the patients were registered by number, stripped, and breech-clotted; their clothes and valuables numbered; their axillary and rectal temperature, their pulse and respiration, and their thoracic, abdominal, and vesical condition noted; and their history registered if obtainable. Catheterization was performed when indicated. It is better to make it a routine measure preparatory to analysis, especially in unconscious cases.

The heat exhaustions were removed to the receiving ward, stimulated with aromatic spirits of ammonia, whiskey, and strychnine, by mouth or hypodermically, according to need, and kept lightly covered. Ice was usually placed at the head, a few were sponged, and a couple required artificial heat. These cases, numbering 35, all recovered.

The heat fevers with temperatures below  $104^{\circ}$  had ice placed at their heads and were showered with water from the hose. As their temperature was reduced they were covered with a sheet, and later removed to the receiving ward. When the heart required it, such stimulation as was given to the heat exhaustions was administered. These cases, numbering 40, all recovered, with one exception, that of a man whose maximum temperature was  $103^{\circ}$ , and whose diagnosis—whether that of alcoholic convulsions or of heat fever with convulsions—still remains in doubt. He died of delirium tremens on the third day and subsequent to apparent convalescence.

The heat fevers with temperatures above  $104^{\circ}$  were given, hypodermically, equal parts of aromatic spirits of ammonia and whiskey, and then placed in a whole bath with ice at their heads and surrounded by floating ice. They were at the same time given a rectal injection of ice water. A finger was kept upon the pulse and the

patient removed when it or cyanosis of the extremities gave alarm; the immersions lasted from four to eight minutes. Twenty-two cases received iced baths, 20 baths without ice, and 1 case was bathed twice. Forty iced enemata were given, and were followed by bowel movements. A fatal case with an initial temperature of  $110^{\circ}$  received five iced enemata. A case that recovered (initial temperature  $110.2^{\circ}$ ) received four of these enemata. They enable the application of cold and fluid internally, and proved a valuable means of supplying these indications. All the patients on removal from the ice-bath to the water-proof cots were more or less cyanosed.

*Ice showering and friction* supplied by ice water driven from a large, coarse, spraying garden syringe, with a maximum of strength, whipped the skin with sufficient force to stimulate the stagnant peripheral circulation, and was aided by surface friction with coarse towels and loofah sponges briskly applied by a couple of attendants. This impact showering and coarse rubbing were most successful in dissipating cyanosis. In some cases, however, it was contraindicated because it aggravated the convulsive tendency. Practically all the cases were showered. There is record of 24 cases with temperatures above  $108^{\circ}$ , and there is record of 24 cases being rough-rubbed. Ice friction (ironing with ice) was also employed.

*Hypodermic medication* was employed with much success. Strychnine, gr.  $\frac{1}{60}$ , one dose administered as a stimulant to the first case, was given to no other for fear of aggravating the convulsive tendency. Aromatic spirits of ammonia and brandy, in equal parts, was much used on thirty-one occasions, digitalis was employed about one-half as often, and ether on but one or two occasions. Atropin, gr.  $\frac{1}{60}$ , was occasionally used as a respiratory stimulant, but principally as a guard to morphine. Morphine was employed for the control of convulsions, in doses of  $\frac{1}{6}$  of a grain, until  $\frac{1}{2}$  of a grain was administered. One case received  $\frac{2}{3}$  of a grain, and a case brought from one of the sugar refineries, and that suffered most violent abdominal cramp, had been given by the attendant there a full grain of morphine. This case, still suffering with cramps, was transferred to the hospital, where the symptom was some time persistent. Its disappearance was followed by toxic symptoms, which yielded to treatment. The morphine, though successfully controlling the con-

vulsive tendency in many cases, failed in others, which were relieved subsequent to, and, it is fair to conclude, in consequence of, bleeding.

*Blood-letting.* Seven cases with temperature ranging from  $109^{\circ}$  to  $110^{\circ}$ , cyanosed and convulsed, were bled at the hospital to the extent of from four to fourteen ounces. An eighth case (temperature  $103.6^{\circ}$ ) was bled on account of cyanosis by Dr. Coplin at the Franklin Sugar Refinery, and then sent to the hospital. Of these 8 cases, 5 recovered and 3 died. Two of the fatal cases were bled during the writer's temporary absence from the sunstroke tent. The pulse immediately prior to bleeding is recorded of one as "too weak to be counted," and the rate of the other was 132. The latter case died twenty minutes subsequent to the bleeding; its maximum temperature was  $111^{\circ}$ . The pulse of the third case at the time of bleeding was 140. An hour subsequent to the bleeding of these 8 cases the pulse was slowed in 4 instances, in 2 it was accelerated, in 1 it was unrecorded, and in 1 it was stopped. In the cases that recovered, the bleeding seemed to relieve cyanosis and convulsive tendency. Blood-letting was not employed until other measures, including morphine, had failed. Both wet-cups and venesection were employed. The blood was obtained with difficulty; it was black and tarry. When cyanosis and convulsion have resisted more moderate measures, or are so pronounced as to demand heroic measures, bleeding is indicated, and, from the experience rehearsed, is preferably limited to the cases that are not without some strength of pulse.

*Camphor suppositories* of 5 grains were employed to meet the convulsive tendency in 2 cases, at the instance of Dr. Henry Fisher, *vice* Dr. Lewis. One case died two hours and twenty minutes after admission, the initial temperature being  $109^{\circ}$ ; the other died of a sequent pneumonia four days after admission. The instances in which the drug was employed are not sufficient to permit conclusions to be drawn concerning its influence in this use of it.

*Turpentine stupes*, in supplement to morphine hypodermically, were employed in some of the cases with marked abdominal cramp persisting after reduction of temperature and restoration of consciousness.

*Oxygen.* Two gallons were given in one case that had a maximum

temperature of  $110^{\circ}$  and that suffered from great respiratory embarrassment and cyanosis. The respiratory rate of 60 was reduced to 32 and the cyanosis overcome in three hours, but six hours later the case proved fatal.

The treatment of the cases reported was guided by constant observation of temperature, pulse, and respiration. When the temperature was reduced to  $102^{\circ}$  or  $103^{\circ}$  the application of cold was stopped and the patient covered. If the temperature rose again treatment was reapplied. After the first great drop of temperature in response to heroic refrigeration, there was always a secondary rise. A few of the cases of moderate fever continued to rise after admission in spite of moderate measures, but were promptly controlled by more decided treatment.

**EFFECTS.** *Curative Effects of Treatment.* The biggest drop in temperature achieved by treatment and with successful result was that of  $11^{\circ}$  F. in one hour and ten minutes. The longest period required for the reduction of high temperature was four hours and fifteen minutes in a case brutally neglected for four hours before being brought to the hospital. The highest temperature reached by cases that recovered was  $110.4^{\circ}$  F., of which there were 2 cases.

<i>Max. Temperature.</i>	<i>Cured.</i>	<i>Died.</i>	<i>Total Cases.</i>
$111^{\circ}$ to $112^{\circ}$ . . . . .	0 cases.	2 cases.	2
110 " 111 . . . . .	4 " "	5 " "	9
109 " 110 . . . . .	2 " "	5 " "	7
108 " 109 . . . . .	5 " "	1 " "	6
107 " 108 . . . . .	3 " "	0 " "	3
106 " 107 . . . . .	2 " "	0 " "	2
$106^{\circ}$ to $111^{\circ}$ . . . . .	16 cases.	13 cases.	29
96 " 106 . . . . .	76 " "	1 case.	77
96- to $111^{\circ}$ . . . . .	92 cases.	14 cases.	106 total cases.

The above table states most conveniently the relation between temperature and recovery.

*The sequels* of immediate origin were 2 cases of pneumonia, 1 of which was fatal, and 3 cases of delirium tremens, 2 of which were fatal. The case of heat meningitis is not classed as a sequel, but as a primary meningitis. Its history will be given in detail in a later publication, and likewise the data of an inquiry into the remote sequels of heatstroke in the cases now reported.

*Mortality.* Fourteen cases of heat fever died. The relation of death to temperature can be studied more conveniently from the accompanying table. The statistics of these 14 fatal cases show that but 1 was a female, the maximum temperature in this case being  $109^{\circ}$ .

<i>Max. Temperature.</i>		<i>Deaths.</i>
108.8 to $111^{\circ}$	13 cases	14 cases.
103	1 case	

The age of 5 cases was between forty and fifty, of 4 between thirty and forty, of 2 between twenty and thirty, and 1 each between fifty and sixty, sixty and seventy, and seventy and eighty years. Six of the 14 cases were of Pennsylvania birth, 7 of foreign, and 1 unrecorded. The foreigners consisted of 3 from Ireland, 2 from Germany, and 1 from Italy. Of the occupations, 8 were indoor, 5 were outdoor, and 1 was unrecorded. The outdoor occupations were all heavy in character, and without exception the vocations of the indoor cases were light.

Of the 14 cases, 3 were admitted moribund, 1 (temperature  $111^{\circ}$ ) dying in five minutes, the second (temperature  $109^{\circ}$ ) in twenty, and the third (temperature  $109^{\circ}$ ), that of an old man of seventy-one years of age, created surprise by remaining alive four hours in response to heroic hypodermic stimulus. Three other cases died of sequels, and 1 of these cases (maximum temperature  $103^{\circ}$ ), the only fatal case with a temperature below  $108.8^{\circ}$ , should rather be classed as a case of alcoholic convulsions. This patient had previously suffered several attacks of delirium tremens, and was on a debauch when admitted, with convulsions; he recovered and was about to be discharged, but delirium tremens developed, which was fatal on the third day. A second case—temperature on admission  $109^{\circ}$ —with a past history of daily indulgence in alcohol, recovered from heat fever, but developed delirium tremens, which was fatal on the eleventh day. A third case of death from a sequel was one from pneumonia on the third day. The patient was large and plethoric, and his past history dealt with alcoholic excess.

In addition to the 3 cases admitted in a moribund condition and 3 that died from sequent trouble, were 2 which had been permitted to go without treatment—one for four hours and the other for many,

but an unknown number, hours before being brought to the hospital. These 8 cases do not represent failure of response to treatment, and yet they comprise more than one-half of the total mortality of 14 cases.

The percentage of the total mortality (14) in a total of 106 cases is 13.2 per cent.

A comparison of percentages of mortality will be made on more equal grounds if limited to the years in which at least 10 cases with a temperature above 108° have been received at the hospital for treatment. These years are but five in number, as indicated by the appended table:

Year.	Heat fever.	Heat exhaustion.	Total cases.	Total mortality.	Per cent. mortality, total cases.	Heat fevers above 106°.	Deaths in heat fevers above 106°.	Per cent. mortality in heat fevers above 106°.
1885	15	16	31	11	35.4 per ct.	12	6	50.0 per ct.
1887	33	11	44	12	27.2 "	25	12	48.0 "
1888	23	5	28	6	21.4 "	11	6	54.5 "
1892	71	35	106	14	13.2 "	29	13	44.8 "
1896	41	38	79	11	13.9 "	25	11	44.0 "
5 years	183	105	288	54	22.2 aver.	102	48	48.3 aver.

A study of the table shows that of the total cases the best percentage of mortality (13.9 per cent.) was obtained in the year 1892, that of the cases now reported. But turning to the cases above 106°, the best result is 44 per cent., obtained in 1896, during the residency of Dr. Starbuck, who, at the suggestion of Dr. Packard, first employed hypodermoclysis at this hospital in the treatment of heat fever. The next best result was obtained by the cases of 1892, now reported. Their percentage was 44.8, which is 0.8 per cent. inferior to that of 1896.

It is the extreme regret of the writer that the imperative claims of succeeding cases and the refusals of relatives denied post-mortem examination in all cases.

CONCLUSIONS. The lessons learned from this experience point not only to what has been gained in the past, but also to what may be done for the future, and perhaps most strongly indicate the necessity for preparedness.

That the percentage of mortality of the cases occurring in 1892 is so much lower than that in the preceding years is probably due to the freer use of fluid and friction as well as of cold. It is not only heat that is to be reduced, but fluid that is to be restored and an embarrassed peripheral and return circulation assisted. The whole bath with ice floating in it, the iced enteroclysis, the hard-impact ice-water showering, the rough and persistent friction—all aided by assistant hypodermic stimulation—are the most responsible factors in the result, and the valuable aids of morphine and bleeding are not to be forgotten.

In 1896 the deficiency in vascular fluid suffered by cases of heat fever was ministered to not only in an additional but also in a much more direct manner by hypodermoclysis, and the result is shown by an improvement of 0.8 per cent. in the mortality of the severe cases.

The most important element of treatment in general for cases suffering from the effects of heat is the *promptness* of its institution. The experimental experience of Dr. Horatio Wood,<sup>1</sup> and the report of Dr. W. M. L. Coplin, referred to in the introductory review (p. 278), establish this beyond doubt.

**PREPAREDNESS.** Hospitals or physicians who have the care of large bodies of men, whether civil (which includes industrial) or military, will be better able to cope with great numbers of patients suffering from heat if, in the spring, preparation is annually made in equipment and assistants for the intelligent and systematic treatment and observation of these cases.

The equipment should include that mentioned in the beginning of this report (p. 285), and, in addition, suitable apparatus for hypodermoclysis. Misconception has arisen from the fact that cases were reported to be treated in a "tent" at the Pennsylvania Hospital. An ordinary tent is a particularly hot and unsuitable place, unless so constructed as to permit the freest ventilation. The screened double awning formerly in use at the hospital better describes what is desirable. It would seem to be of advantage if the inside of the canvas were

<sup>1</sup> Discussion of paper by Dr. Hopwitz, TRANSACTIONS OF THE COLLEGE OF PHYSICIANS, Philadelphia, 1885, 3d S., viii. 195.



tinted green; the glare in a white tent can be most distressing. Assistants pledged to the examination of urine, blood, reflexes, eye-grounds, to say nothing of physical conditions, would add much to the exact treatment of these cases and contribute scientific information concerning them that is still unrecorded. Carefully tabulated blanks of symptoms and treatment will aid much in this regard, and must be prepared beforehand.

In conclusion, the writer makes grateful acknowledgment of the generous help accorded him in the treatment of these cases by Drs. Charles Williams, Morris B. Miller, Richard Wilson, John H. Gibbon, and Dr. then Mr. William R. Nicholson; and in the after-treatment by Drs. Thomas Branson and Thomas Ash Claytor.

Finally, the writer would revert to the question of terminology, and state the need he has felt of a generic term embracing the three recognized forms of pathological effect from heat. The word "heat-stroke" employed by Dr. Levick is the term of broadest signification that has been used, and both historically and from the meaning of its component words—though the latter one is a little dramatic—is, nevertheless, perhaps the best available to be applied to and to comprise the three species of heat effect: heat exhaustion, heat meningitis, and heat fever.

## DISCUSSION.

DR. MORRIS J. LEWIS: I believe that the increased number of cases during later years, as shown by Dr. Spellissy's tables, has been influenced by the larger number of persons occupied each year in the different trades; and I also believe that the statement made that foreigners are more liable to the effects of heat than native Americans is influenced by the fact that there are more foreigners than Americans employed in occupations requiring heavy labor during the heated term. In my experience I have had three cases to reach a temperature of  $111^{\circ}$  and recover. This temperature had, however, to be guessed at, the thermometers registering only a little above  $110^{\circ}$ , but the mercury rose a full degree, by measure, above the latter figure.

In my estimation it is not the high temperature alone that causes the bad effects, but the continued high temperature, with high humidity for a number of days, during which time the patients have had to be at work. If, during the progress of this hot spell, Sunday intervenes, the number of

cases is not so large. It is the continued hot weather for several days, with hard work and no holiday, that causes a large number of cases.

In several of the cases that I have seen a condition occurred that I cannot explain. One of them, a man, was sunstruck in the middle of the day, and when he recovered he could not remember anything that had occurred in the morning. He was told by his wife of several important events that he had participated in that morning, but he could not recollect any of them.

I have nothing to add to what Dr. Spellissy has said, but should like to see the treatment used that has recently been advocated—viz., hypodermoclysis. I have not yet had an opportunity of trying its effect. I have always heretofore been satisfied with cold applications.

At the Pennsylvania Hospital the records are, unfortunately, incomplete, and have to be so, unless a resident is appointed especially to note the symptoms of the patients. There is much of this work yet to be done which cannot be properly attended to if the resident is expected to look after the treatment as well. Careful blood examinations, etc., should be made in every case.

DR. H. M. FISHER: I happened to be substituting at the Pennsylvania Hospital for a week or two during the very hot weather of 1892, when Dr. Spellissy was resident physician, and he deserves great praise for the energetic and conscientious work that he performed under the most trying circumstances. It seemed to me that the ambulance gong was sounding every five minutes for at least a week while I was on duty there. I am sorry to say, however, that I have no personal observations of value to record regarding the treatment of thermic fever. When I was resident physician at the Pennsylvania Hospital, in the summer of 1878, there were, I think, seven or eight sunstroke cases treated. The patients were treated in the old receiving ward, where the facilities for ice-water applications were not very good, and the results were not so good in consequence as they have been in more recent years.

It must be a matter of regret that Dr. H. C. Wood, who has written an extremely interesting monograph on thermic fever, is not present with us to-night to take part in this discussion.

The question of the cause of death in these cases is an interesting one. The observation has been made a number of times that the coagulability of the myosin in the muscles increases after death; but in the various experiments undertaken by Dr. Wood he was able to prove that the process began just before death, and that in almost all cases there was marked rigidity of the heart muscle. This was probably due to the increased coagulability of the myosin, caused by the extreme heat. We may therefore, I think, fairly assume that the fatal result may at least in part be due to this change in the heart muscle, though Dr. Wood is of the opinion that in most cases it is a respiratory death rather than an ordinary death from syncope, and that

the profound impression produced on the cerebral ganglia by the extreme heat is the primary cause of death.

In that connection the question of intravenous injections of salt solution is interesting. Dr. F. A. Packard has called attention to the marked benefit resulting from these intravenous injections, and they unquestionably do have a beneficial effect in many cases. In some experiments made by Dr. Wood on animals he found that the intravenous injections of normal salt solution very markedly retarded the coagulation of the myosin and the consequent rigidity of the muscles, and more particularly of the heart muscle.

DR. J. C. WILSON: The paper of Dr. Spellissy is a most interesting communication, as it not only gives a progressive historical study of the clinical facts in regard to thermic fever and heat exhaustion, but it also shows the large part taken by the Pennsylvania Hospital and those connected with it from time to time in extending our knowledge upon this subject. I regret that Dr. Spellissy did not indicate the occupations of the individuals whose cases are studied, because it seems to me that this has a good deal of bearing upon the subject of thermic fever and heat exhaustion, and suggests a theory, or working hypothesis, in regard to the nature of the former. It would appear that the attacks not only occur during hot weather, but that they especially also occur in working people or laborers chiefly, as pointed out by Dr. Spellissy, at the time of day when the workman is most busily engaged at his occupation. The suggestion for the working hypothesis is that not only is death due to some profound change in the muscular mass, but that the symptoms must be largely due to auto-intoxication from this source, and that the extreme elevation of temperature, the nervous symptoms (including the convulsions), and the changes analogous to the cadaveric changes in muscle, which go to make up the pathological series of events in these cases, are the result of a sudden profound derangement of the retrograde metamorphosis of muscular tissue. There is some analogy in the conditions found after death with those found in cholera, although the convulsions that occur in thermic fever do not occur in cholera; those occurring in thermic fever are mostly clonic, while those in cholera are tetanoid.

The method of treatment by hypodermoclysis, to which attention has been called by Dr. Fisher, was dwelt upon in an article written by Dr. Packard for a work on therapeutics which I edited some years ago—viz.: *A Text-book of Applied Therapeutics*. From this time on it seems to me that no severe case should, in the present state of our knowledge, be regarded as properly treated if measures of this kind are not employed. The analogy between the condition of the blood itself and the bloodvessels, and that of the blood in cholera, is emphasized by the anuria characteristic of the initial period of thermic fever. The distinction between thermic fever and heat exhaustion is a radical one, the symptoms in heat exhaustion not

being those of nerve excitement, but of nervous exhaustion and intense fatigue, and occurring in individuals in whom muscular exercise has not been active, as is mostly the case in those suffering from thermic fever.

DR. F. A. PACKARD: There are one or two features about thermic fever which, while they are minor ones, might, in my opinion, receive more attention than is usually given to them in the text-books. One of the most characteristic features of a case of sun-stroke is the curious odor, which is peculiar, and could be best described by being at the same time "mousy" and cadaveric. I have never noticed exactly this same odor in any other condition. The patient with thermic fever usually keeps up a continuous droning groan, which also is characteristic. The convulsions in thermic fever sometimes more resemble a rigor than a true convulsion. The whole body is in a state of tonic spasm, with marked flexion of the arms at the elbows, and there is besides this constant rhythmical clonic spasm, resembling almost precisely that seen in a severe chill. The stools also in thermic fever are characteristic, being watery, with slight odor, and containing many thin flakes made up of groups of intestinal epithelial cells.

While resident physician in the Pennsylvania Hospital in 1887 I bled many of the cases, with, I am sure, advantage to most of them. This I did in spite of the fact that the pulse at the wrist was feeble, and in many cases, as the blood flowed from the vein, the radial pulse improved in volume. It seemed as though in these cases most of the blood of the body was contained in the venous side of the circulation. It seems to me that a small pulse is no contraindication to the letting of blood in these cases, as the condition is entirely different from that seen where the feeble pulse is due to loss of blood or exhausting disease. After cutting the median basilic vein it is frequently noticed that the blood can be made to flow only with great difficulty, apparently because of the great viscosity of the blood. This was so great that pressure had almost always to be made from the hand up to the point of incision. As the blood came from the wound it was seen to be almost grumous. After leaving the hospital I did not again see, so far as I remember, a case of this kind until 1898. One hot August morning of that year I was sent for to see a patient of mine at his house. He had been feeling badly all night, following three days of great discomfort from the heat. In the morning when I saw him he felt hot and uncomfortable, and complained that he was unable to perspire. He had a good deal of headache and a temperature of 102°. Scattered all over the body there was a red papular eruption, which was found to have its seat at the mouths of the sweat-ducts. I prescribed citrate of potash mixture, recommended perfect quiet, and advised him to take plenty of fluids through the day. Late that evening, on my return from a visit to the country, I found a message asking me to come and see him, and, on arriving, found him with a temperature of 111° and a typical attack of thermic fever. In spite of everything that I could do through the night he

died the next morning. The two things that struck me most in regard to his case were his complaint of inability to perspire and the curious injection about the sweat-ducts.

A few summers ago a man was brought into the Pennsylvania Hospital with a typical attack of thermic fever. I saw him not long after his admission, when he was comatose and convulsed, with stertorous breathing and pin-point pupils. Twelve ounces of blood were removed from the arm, with the result that his moaning ceased and the convulsive movements stopped. While I watched the resident physician bleeding him I was again struck with the apparent viscosity of the blood. As the patient still remained unconscious I had a pint of normal saline solution introduced under the skin in the pectoral region. Before the fluid was entirely absorbed the man opened his eyes and asked where he was. This happens to have been the last case of sunstroke that I have seen, so that it is the only one that I can report wherein hypodermoclysis was used.

I believe that many at least of the symptoms of thermic fever may be due to the absence of a sufficient amount of watery material within the blood. The facts pointing to this possibility are: that cases of thermic fever do not occur until a hot term has lasted more than three days; that it is usually found that during these three days the patient has been sweating profusely; that the case that I have mentioned above had hyperæmia about the mouths of the sweat-ducts; and that in one case which I have mentioned hypodermoclysis at least seemed to be productive of good results so rapidly as to be almost startling to the on-lookers.

I have been unable to follow the subject up because of lack of material recently. This could readily be done, and proof positive obtained as to the condition of the blood in thermic fever. I have, however, asked Dr. Longcope, the resident pathologist at the Pennsylvania Hospital, to see if something definite cannot be learned this summer in regard to the specific gravity of the blood and the number of red cells per cubic millimetre in any cases that may occur during the coming summer. If it were possible it would also, it seems to me, be of value to determine whether the serum obtained from these cases might not contain more toxin to the cubic centimetre than would be the case in normal blood. As Dr. Wilson has suggested, toxins very likely play a large part in the production of symptoms.

Among the cases that I treated in 1887 one stands out prominently, because it was not a case of thermic fever. One hot August afternoon, when cases of sunstroke were coming into the hospital in rapid succession, an old man was brought in by the police, who had picked him up in the street in an unconscious condition. He was hurriedly examined, found to be semi-conscious, with a temperature of 106°. He was looked upon as a case of thermic fever, and promptly ironed with ice. His temperature soon fell to normal, and that evening he was allowed to go home. He returned, however, two afternoons after his first admission, when more time was at

my disposal for studying cases, and I found that while his temperature was at 106° again, he had also an enlarged spleen, and he confessed to living in a town a little above this city on the Delaware River. This is one of the great dangers during the hurry necessarily present, even with the best arrangements, when thermic fever cases are coming into a hospital in large numbers. I think that the malarial paroxysm would be the most likely to be the source of error, because of the fact that in this climate malaria and thermic fever are both rife at the same time. While the old gentleman whose case I have mentioned was not injured by his hydrotherapeutic treatment, it would have been more to his benefit and to my credit had he been given a hypodermic injection of bismuriate of quinine and urea in place of or in addition to his bath.

DR. JAMES TYSON: I want to add only one point in explanation to the effect of submersion in sunstroke, as contrasted with simple cold friction with ice. In submersion there is a certain amount of absorption taking place. When the blood is thickened and drained of its water, absorption through the skin takes place readily. In this way we have a substitute for hypodermoclysis or intravenous injection. The cases recover more rapidly when immersed in a bath than when rubbed with ice; therefore, I believe it is reasonable to believe that the relief is obtained by absorption through the skin.

DR. PACKARD: From what I have heard I think that I hardly made myself plain in regard to the use of bleeding and hypodermoclysis. I do not believe that bleeding is a necessary preliminary to the use of hypodermoclysis, and would prefer using the latter remedy first, keeping in reserve the letting of blood in case it might be necessary. Of the two measures, I should think that hypodermoclysis might be the more valuable.

DR. JOSEPH M. SPELLISSY concluded the discussion, and expressed his thanks for the free and valuable discussion accorded his paper, which, he believed, when read in its entirety, would be found to affirm many observations and beliefs expressed by those who honored the paper by discussing it. The statistics of occupation in which Dr. Wilson had expressed interest were noted in the Report, but they, and, in fact, the greater part of the Report were omitted in reading, because so much time had been devoted to the presentation of the Historical Review. The identification of the staff of the Pennsylvania Hospital and of the Fellows of the College of Physicians with the early history of the treatment of the effects of heat suggested that this matter might be of greater interest to the meeting. In conclusion, the necessity of hospitals and of physicians who have the care of large bodies of people, making yearly preparation for the treatment of heat-stroke, was repeated and emphasized.



## APPENDIX.

### ABSTRACT OF THE REPORT OF THE COMMITTEE ON MÜTTER MUSEUM, 1901.

One hundred and fifty specimens were added to the Museum, as follows:

Necrosis of Lower Jaw. Presented by Dr. John B. Roberts.

Congenital Hypertrophy of Skin of Face and Head; Right and Middle Lobes of Prostate Gland; Posterior Prostatectomy. Presented by Dr. John B. Roberts.

Skiagraphs of Stave of Thumb, or Bennett's Fracture of Metacarpal Bone of Thumb. Presented by Dr. John B. Roberts.

Skiagraphs of Old Fractures, Lower End of Radius. Presented by Dr. John B. Roberts.

Skiagraphs of Fractures of Lower End of Radius, with Forward Displacement (Smith's Fractures). Presented by Dr. John B. Roberts.

Cast of Five Fractures of Lower End of Radius, with Forward Displacement. Presented by Dr. John B. Roberts.

Tumors from Sciatic Nerve and Internal and External Popliteal (Fibroma). Presented by Dr. John B. Roberts.

Congenital Tumor of a Child, aged Six Weeks, Removed from Coccygeal Region. Presented by Dr. John B. Roberts.

Vesical Calculi. Presented by Dr. John B. Roberts.

Tarsectomy, with Fragments Removed. Presented by Dr. John B. Roberts.

Appendix. Presented by Dr. John B. Roberts.

Photographs of Keloid Tumors. Presented by Dr. John B. Roberts.

Photographs of Congenital Anterior Luxation of Tibia (five photographs). Presented by Dr. John B. Roberts.

Tubercular Bodies Taken from a Cyst in the Groin. Presented by Dr. De Forest Willard.

Skiagraph of Separation of Epiphyseal Crust of Calcaneum. Presented by Dr. De Forest Willard.



Pedicated Fibroma of both Ovaries. Presented by Dr. Richard A. Cleemann.

Cancer of Fundus Uteri. Presented by Dr. J. M. Baldy.

General Dropsy of Fœtus, with Placenta. Presented by Dr. Daniel Longaker.

Specimen of Encysted Hydrocele of Cord. Presented by Dr. Orville Horwitz.

Multilocular Cyst of Testicle. Presented by Dr. W. L. Rodman.

Goitre. Presented by Dr. W. L. Rodman.

Appendix, with Enterolith. Presented by Dr. W. L. Rodman.

Cyst from Submaxillary Region. Presented by Dr. W. L. Rodman.

Resection of Saphenous Vein. Presented by Dr. W. L. Rodman.

Adherent Vesical Calculus. Presented by Dr. W. L. Rodman.

Large Myoma of Uterus. Presented by Dr. W. L. Rodman.

Lipoma of Back. Presented by Dr. W. L. Rodman.

Hernial Sac and Omentum. Presented by Dr. W. L. Rodman.

Ligamentous Preparations of Foot after Excision. Presented by Dr. James K. Young.

Amputation of a Knee after Excision. Showing Line of Union. Presented by Dr. James K. Young.

Calvaria of a Typical Case of Osteitis Deformans, with Photograph. Presented by Dr. Frederick R. Packard.

Specimen of Dry Gangrene of Right Forearm, showing Line of Demarcation. Presented by Dr. W. J. Taylor.

Dr. Oscar H. Allis has contributed over one hundred specimens of fractures of shoulder, elbow, wrist, knee, hip, patella, and ankle. These form a wonderful collection of joint injuries, twisted fractures, so-called sprains, luxation fractures, ankle sprains, Colles', Pott's, and fissured fractures. These artificial fractures are intended to show the great internal destruction accompanying fractures near joints which may occur without distinctive external symptoms. This collection is worthy of the closest study; the specimens are revelations of surgical pathology. It is proposed to mount them in flat cases, so that they can be studied to the best advantage.

The committee state that the revision of the Museum Catalogue is being actively carried on, and a card index catalogue is being prepared by which every specimen can be instantly located in its proper case and shelf, and its exact position recognized from the floor of the Museum hall. The Curator states that upon notification he will be glad to remove from the cases to the study tables in the hall any specimen or sets of specimens which any Fellow may require for reference or study.

In conclusion the committee earnestly draw attention to the necessity of continual contributions to the Museum. They beg the Fellows to bear in mind that when a specimen is deposited in the Museum it is not lost to the depositor, but is at all times subject to the owner's order.

On notification to the Curator of the Museum or to the Janitor of the College the Museum will send at once to the house of the depositor, to a hospital, or to any designated place for any specimen to be donated or deposited in the Museum. The Curator particularly desires it to be understood that he will at all times hold himself in readiness to facilitate in every way the use of the Museum by the Fellows of the College.

## SUMMARY OF THE REPORT OF THE LIBRARY COMMITTEE FOR 1901.

THE number of volumes now in the library is 64,916, an increase during the year of 3557.

The General Library contains	.	.	.	.	.	48,646
“ Lewis “ “	.	.	.	.	.	12,984
“ Gross “ “	.	.	.	.	.	3,069
“ Obstetrical Society “	.	.	.	.	.	217

This number includes 1970 duplicates retained as reserves to supply the place of journals and other volumes most frequently consulted when they are worn out by constant use. All other duplicates are disposed of as rapidly as possible. 479 have accumulated since July, when all on hand were disposed of. \$860.74 was received from the sale of duplicates during the year, besides \$86.81 to our credit with the New York Medical Book Co. In addition to the volumes, there are 58,395 unbound pamphlets, reports, and transactions.

The Library receives regularly, by purchase and exchange, 356 medical periodicals, 86 American and 270 foreign (55 more than during 1900), and in addition 247 American and 124 foreign current numbers have been presented, chiefly through the courtesy of editors.

Forty-six journals were added to the subscription list during the year, and it is hoped that a further addition of at least thirty-five can be made in January.

2212 inaugural dissertations have been received.

There were 211 donors during the year, of whom each of the following donors has presented more than 50 volumes:

Bequest of Dr. John Ashhurst, Jr.	.	.	.	.	1500 volumes.
Bequest of Dr. Alfred Stillé	.	.	.	.	207 “
Dr. T. G. Ashton	.	.	.	.	178 “
Dr. George Fales Baker	.	.	.	.	167 “
Dr. H. A. Hare	.	.	.	.	113 “
Dr. J. K. Mitchell	.	.	.	.	106 “
Dr. S. Weir Mitchell	.	.	.	.	95 “
Dr. L. S. Clark	.	.	.	.	92 “
Dr. Francis R. Packard	.	.	.	.	83 “
Dr. E. P. Davis	.	.	.	.	72 “
Dr. W. B. Atkinson	.	.	.	.	54 “

The Library is also indebted to the publishing houses of Blakiston, Saunders, Lippincott, Davis, and Lea for gifts of new publications, and to many of the Fellows for a great number of journals and pamphlets.

Thirty-six of the new publications added to the Library have been written or edited by Fellows of the College.

In April last the valuable collection of rare books made by the late Dr. J. Stockton Hough was offered for sale, and many Fellows of the College were very desirous that it should be procured for the Library. The energetic action of the President of the College, who made a personal visit to New York, and the liberality of Dr. George Fales Baker, who contributed \$500, Dr. S. Weir Mitchell, who contributed \$300, and Dr. J. K. Mitchell, who contributed \$200, made it possible, with the additional funds at the disposal of your Committee, to secure the collection. It consisted of 3247 volumes and 2070 pamphlets, reprints, etc., and included rare and valuable works on medicine, bibliography, etc., many of them of very old date. To determine which were non-medical works or duplicates each was examined by the Honorary Librarian and Librarian, and compared with the catalogue of the Library, and 1500 volumes and 1039 pamphlets were retained. Some of the more important pamphlets were bound in 49 volumes, making an addition of 1549 books to the Library. The following statement by the Librarian will give some idea of the great value of this collection. "515 of the volumes were printed before the year 1700. 76 (known as incunabula) were printed in the fifteenth century, 175 in the sixteenth, and 264 in the seventeenth. Of the rarity of some of them, the following titles, with accompanying notes by Dr. Hough, will afford an illustration:"

Bernard de Gordon. *Fleur de Lys en Médecine*. Lyon, 1495. Sm. fo. [An exceedingly rare book. The first and only edition in French in the fifteenth century. Purchased for 117 marks.]

Joh. Ketham. *Fasciculo di Medecina vulgare*. Venetia, 1508. Sm. fo. [Only two copies known of this edition, this and one in the Public Library of Venice. It is rarer than any Latin or Italian edition of the fifteenth or sixteenth centuries. Purchased for 300 francs.]

Simon Genuensis. *Synonyma*. Milan, 1473. [First edition of the first medical dictionary. Extremely rare. Purchased for \$11.00.]

Benevenuti Grassi. *De Oculis Eorumque Egritudinibus & Curis Feliciter Incipit*. [Ferrariae, 1474.] Sm. 4to. [First edition of the first book printed on diseases of the eye. It is of extreme rarity. Cost 110 francs.]

Ambrose Paré. *Briefve collection de l'Administration Anatomique*. Paris, 1550. 12mo. [On the flyleaf of this book, written in French in 1867, and signed Munaret, are a number of notes showing the rarity of this work. He first mentions that Malgaigne had only been able to discover two copies. Of this edition, one slightly mutilated, the property of M. Champion de

Bar-le-Duc, the other, a fine and complete copy, in the Bibliothèque Mazairain, No. 29,797. He then goes on to say that while hunting for an old book in Lyon he discovered this third copy, and after having collated and compared it with the one at Paris, he is bold enough to say that it is its equal, and further on, that the "restoration" of this precious volume has been made by Bruyère (one of the famous French binders) at a cost of 40 francs. The work is bound in crushed Levant morocco, outside plain, inside gold tooling.]

Dioscorides. *De Materia Medica*. Colle, 1478. fo. [First book printed at Colle. Cost 500 marks.]

Bagellardus. *De Infantium aegritudinibus et remedis*. Patavii, 1487. Sm. 4to. [The second edition of the first book printed on the diseases of children. (First edition, 1472.) Cost 50 marks.]

Champerius. *Index librorum in hoc volumine contentorum*; Symphoriani Champerii libelli duo. *Primus de medicinae claris scriptoribus in quinque partibus tractatus*. [Lugduni, 1506.] Cost \$35.00. [An extremely rare book. The first edition of the first medical biography, also bibliography, published.]

Isaac. *Tractatus de particularibus diaetis*. Padua, 1487. [An exceedingly rare book. First edition of the first book printed on diet.]

Johannes Peyligk. *Philosophiae Naturalis*. Liptzensi, 1499. fo. [The first book published with anatomical plates of individual organs. These plates copied from the edition 1498 of Mundinus. This is one of the rarest of rare books, worth at least \$100. I have never seen it in any catalogue or elsewhere for sale. Stockton Hough, 1900.]

The non-medical and duplicate books of the collection were disposed of in October to the Library of the University of Pennsylvania for \$1500.

The number of visitors to the Library during the year was 4596, 185 less than during 1900. 12,462 books were furnished by the Librarian for consultation in the Library, 2020 more than during last year, and many more were taken directly from the shelves by Fellows of the College. 2556 books were taken out, an increase of 145.

Fellows engaged in research in the Library have been greatly inconvenienced by the discontinuance of the *Index Medicus* of the Surgeon-General's office. The *Index* published in Paris has been found a very unsatisfactory substitute, and, moreover, seems likely to be discontinued also. The Librarian has suggested that a card index could be formed if cataloguers could be employed to subject-index all original articles and clinical lectures in the journals received by the College; the cards to be kept in a separate case and the indexing to be continued back to the period when the publication of the *Index Medicus* ceased. The interest of a fund of \$20,000 or \$30,000 would be needed.

At the risk of wearying the Fellows with endless reiteration, your Committee must refer again to the ever-recurring subject of shelving, which will not down. With the books stored in nine different rooms and five galleries, the classification and numbering repeated in three libraries, the room even for storage wellnigh exhausted, and a flood of new books always pouring in, Fellows who use the Library much and are familiar with its working will appreciate the labor, care, and skill required on the part of the Librarian and his assistants to prevent the Library from falling into inextricable confusion. The congestion will be temporarily somewhat relieved by the use of the cases in the committee room and the space above the toilet room, which will make it possible to store the books, though at great inconvenience at their average rate of increase, for about two years; but it is only too evident that it will be absolutely necessary to do something radical in the way of increasing the capacity of the College building in the near future. Our Library is believed to rank third among the medical libraries of the world, and is a valuable possession of which the Fellows of the College may well be proud.

GEORGE C. HARLAN, M.D.,  
*Chairman.*

## LIST OF PAPERS: SECTION ON OPHTHALMOLOGY.

*December, 1900.*

A Case of Myosis and Ptosis Due to Gunshot Injury of the Right Cervical Sympathetic Received Five Years ago, by Dr. G. C. Harlan.

A Case of Subluxation Downward and Inward of Each Lens, by Dr. James Thorington.

Restoration of Useful Vision in a Complicated Case of Acute Inflammatory Glaucoma of Ten Days' Duration, with Visual Acuity Reduced to the Perception of Light, by Dr. C. A. Veasey.

Tuberculosis of the Conjunctiva in a Healthy Child Thirteen Years of Age, by Dr. H. F. Hansell.

A Piece of Iron Embedded in Inflammatory Exudate Removed from the Vitreous by Forceps after Failure of Magnet, by Dr. William M. Sweet.

*January, 1901.*

A Case of So-called Inflammatory Coloboma, by Dr. John T. Carpenter.

A Case of Exophthalmos, the Result of Osteoporosis, by Dr. P. N. K. Schwenk (by invitation).

Carcinomatous Degeneration of a Papilloma of the Bulbar Conjunctiva, by Drs. S. D. Risley and E. A. Shumway.

A Case of Inflammatory Glaucoma Presenting Unusual Features, by Dr. S. D. Risley.

A Case of Glioma of the Retina, by Drs. M. W. Zimmerman and B. K. Chance.

A Case of Circinate Retinitis, by Dr. G. E. de Schweinitz.

Technique of the Hotz-Anagnostakis Entropion Operation, by Dr. G. C. Harlan.

*February, 1901.*

A Case of Synchysis Scintillans, by Dr. William Zentmayer.

A Case of Paresis of the Left Internal Rectus Following Diphtheria, by Dr. G. Oram Ring.

Melanotic Sarcoma of the Choroid, by Dr. John T. Carpenter.



Binocular Hemianopsia and Optic Nerve Atrophy in a Case of Diabetes Mellitus, by Dr. H. F. Hansell.

A Case of Black Cataract, by Dr. S. D. Risley.

Extraordinary Calcareous Deposit in the Tarsal Conjunctiva, by Dr. S. D. Risley.

Some Unusual Choroidal Lesions Associated with Pregnancy, by Dr. G. E. de Schweinitz.

A Case of Normal Combined Cataract Extraction, in which the Anterior Chamber was not Re-formed until the Thirty-second Day, by Dr. G. E. de Schweinitz.

*March, 1901.*

A Case of Recurring Hemorrhage in the Anterior Chamber, by Dr. B. Alex. Randall.

A Case of Degeneration of the Pigmentary Layer of the Retina, by Dr. G. C. Harlan.

Results of Extraction of Steel from Vitreous, by Dr. William Thomson.

Three Cases of Intoxication Amblyopia with Retinal Hemorrhages, by Dr. William Zentmayer.

Rupture of the Sphincter of the Iris and V-shaped Rupture of the Choroid, by Dr. G. E. de Schweinitz.

Three Cases of Rupture of the Iris from Contusion of the Eyeball, by Dr. William M. Sweet.

Subconjunctival Dislocation of the Lens, by Dr. G. E. de Schweinitz.

Treatment of Pterygium by the Szokalski Ligature, by Dr. G. C. Harlan.

*April, 1901.*

Right Oculomotor Paralysis and Left Trifacial Paralysis, by Dr. C. A. Veasey.

A Case of Abscess of the Orbit from Diseases of the Ethmoid; Curetting Through the Orbit and Drainage Through the Nose, by Dr. G. C. Harlan.

Iridectomy in Case of Obliteration of the Anterior Chamber, by Dr. G. C. Harlan.

Hæmophilic Extravasation into the Conjunctiva, Antrum, and Cheek, by Dr. S. Lewis Ziegler.

Recurring Hemorrhages from the Ciliary Body, by Dr. S. Lewis Ziegler.

Purulent Choroiditis, by Dr. John T. Carpenter.

Use of Pilocarpine in the Treatment of Inflammations of the Eye, by Dr. H. F. Hansell.

A Case of Methyl-alcohol Amaurosis, the Pathway of Entrance of the Poison being the Lungs and Cutaneous Surface, by Dr. G. E. de Schweinitz.

New Lantern Test for Detecting Color Blindness, by Dr. William Thomson.

*October, 1901.*

Blindness from Congenital Deformity of the Occiput, by Dr. Charles A. Oliver.

Three Cases of Relapsing Traumatic Bullous Keratitis, by Dr. G. E. de Schweinitz.

The Thorner Stationary Ophthalmoscope, by Dr. H. F. Hansell.

The Hirschberg Sideroscope, by Dr. William M. Sweet.

WILLIAM M. SWEET,  
Clerk of Section.

## LIST OF PAPERS: SECTION ON OTOTOLOGY AND LARYNGOLOGY.

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Treatment of Chronic Laryngitis, by Dr. P. S. Donnellan.

Mastoid Operations, by Dr. George H. Stout.

On Localization of Sound, with Especial Reference to Unilateral Deafness, by Dr. B. Alex. Randall.

Report on Nasal Septum as Found in Skulls of Forty Mound-builders, by Dr. George B. Wood.

Notes on a Case of Excised Jugular Sinus, by Dr. B. Alex. Randall.

Treatment of Saddle-back Nose by the Insertion of a Gold Plate (illustrated by patient, skia-graph, and plaster model), by Dr. E. B. Gleason.

Report on a Case of Idiopathic Hemorrhage from the Larynx, by Dr. George B. Wood.

Retropharyngeal Abscess, with Report of a Case, by Dr. Jos. S. Gibb.

Operations for Mastoid Disease (by invitation), by Dr. Clarence J. Blake, of Boston.

A Radical Mastoid Operation upon an Infant of Six Months, by Dr. Charles H. Burnett.

Notes on Some Recent Mastoid Operations, by Dr. B. Alex. Randall.

Brief Report on Recent Mastoid Operations, by Dr. Arthur Ames Bliss.

Remarks on Recurrent Papilloma of the Larynx and on the Means of Preventing Such Recurrence, by Dr. E. L. Vansant.

An Unusual Case of Sinus Disease, by Dr. Arthur Ames Bliss.

Results of a Mistake in Putting up a Prescription for Adrenalin Chloride to be Used as a Nasal Spray, by Dr. Charles H. Burnett.

Hemorrhagic Myxoadenofibroma of the Nasopharynx, by Dr. Alex. W. MacCoy.

Fibroma of Nasopharynx, with Sarcomatous Areas, by Dr. Alex. W. MacCoy.

Recurring Polypus of the Nose, by Dr. George Morley Marshall.

Result of Mastoid Operation, by Dr. E. B. Gleason.

Case Illustrating Results of Injury to Nasal Bones, by Dr. E. B. Gleason.

A Case of Pharyngitis Caused by Rhus Toxicodendron, by Dr. Arthur B. Watson.

Syphilitic Ulceration of the Pharyngeal Vault, by Dr. P. S. Donnellan.

A Case of Stenosis of the Larynx, by Dr. Arthur Ames Bliss.

Exhibition of New Instruments, by Dr. E. L. Vansant.

Traumatic Deformity of Nose, with Operation, by Dr. P. S. Donnellan.

Sequestrum from Auditory Canal of Two-year Old Child, by Dr. Charles H. Burnett.

A Case Illustrating Method of Operation and Results of Treatment in Mastoid Caries, with Abscess, by Dr. E. B. Gleason.

Recent Rupture of Drumhead Treated by Application of Blake's Paper Patch, by Dr. Joseph Price Tunis (by invitation).

Fibroid Growth in the Larynx, by Dr. Walter Roberts.

Papilloma of Right Vocal Cord, by Dr. E. L. Vansant.

FRANK WOODBURY,

Clerk of Section.

## LIST OF PAPERS: SECTION ON GENERAL MEDICINE.

DECEMBER 1, 1900, to DECEMBER 1, 1901.

### *Papers Read.*

- Report of a Case of Malignant Endocarditis, by Dr. D. J. Milton Miller.  
The Association of Chronic Jaundice, with Gastropptosis, with the Report of a Case and the Exhibition of the Patient, by Dr. J. Dutton Steele.  
Two Cases of Aortic Disease, with Specimens, by Dr. Joseph Sailer.  
A Complicated Case of Facial Palsy, by Dr. William G. Spiller.  
Methods of Examining the Gastric Contents, by Dr. D. L. Edsall.  
Vascular Degeneration as a Family Disease and its Relation to Migraine, by Dr. D. J. McCarthy.  
Primary Tuberculosis of the Pericardium, by Dr. David Resman.  
A Case of Endocarditis Resulting from Typhoid Fever, by Dr. J. A. Scott.  
A Patient with Marked Enlargement of the Liver and Spleen, by Dr. A. O. J. Kelly.  
A Case of Aneurism of Thirteen Years' Standing Recently Successfully Operated upon for the Removal of a Huge Cyst of the Broad Ligament, by Dr. S. McC. Hamill.  
A Case of Aortic Regurgitation, with Flint Murmur, by Dr. Joseph Sailer.  
A Case of Median Nerve Paralysis from a Gunshot Injury, by Dr. William G. Spiller.  
Use of Gelatin for the Arrest of Hemorrhage, and A Contribution to the Clinical Manifestations of Exophthalmic Goitre, by Dr. Joseph Sailer.  
Splenic Anæmia, by Dr. D. D. Stewart.  
Report of a Case of Aneurism of the Arch of the Aorta which Ruptured into the Pericardium, by Dr. J. A. Scott.  
A Case of Malignant Endocarditis and Brain Abscess, with Unilateral Kernig's Sign, by Dr. Joseph Sailer.  
Iodic Purpura, by Dr. Alfred Stengel.  
A Discussion by Drs. F. A. Packard, J. P. Crozer Griffith, Alfred Stengel, and J. K. Mitchell upon Methods of Keeping Case Records in Private Practice.

Two Cases of Aneurism of the Descending Portion of the Arch of the Aorta, by Drs. Sailer, Pfahler, and Shields.

A Case of Acromegaly, by Dr. A. A. Eshner.

Experimental Investigation into the Causes and the Treatment of Diabetes Mellitus, by Dr. Alfred C. Croftan, by invitation.

*Cases Shown.*

A Case of Probable Localized Interlobar Pleurisy, by Dr. F. A. Packard.

A Case of Chronic Jaundice, with Gastropotosis, by Dr. J. Dutton Steele.

A Case of Right Facial Palsy followed by Transitory Paralysis of the Right Upper Limb, by Dr. William G. Spiller.

A Case of Traumatic Paralysis of the Infra-orbital Division of the Fifth Nerve, by Dr. Henry M. Fisher.

A Case of Arthropathy without Symptoms of Spinal-cord Disease, by Dr. Joseph Sailer.

A Case of Aneurism of the Descending Portion of the Aorta, by Dr. J. A. Scott.

(1) A Case of Amyotrophic Lateral Sclerosis of the Scapulohumeral Type; (2) A Case of Isolated Paralysis of the Anterior Tibial Muscle, by Dr. William G. Spiller.

A Case of Spleno-myelogenous Leukæmia, with a Greatly Enlarged Spleen, by Dr. D. J. Milton Miller.

An Atypical Case of Disseminated Sclerosis, by Dr. William G. Spiller.

An Interesting Case of Aneurism, by Dr. H. A. Hare.

(1) A Patient with a Condition Simulating Carotid Aneurism; (2) A Case of Pernicious Anæmia with Peculiar Pigmentation of the Skin, by Dr. F. A. Packard.

(1) A Patient with Amytrophic Lateral Sclerosis of Unilateral Type; (2) A Case Showing Increase of the Supra-orbital Reflexes, by Dr. D. J. McCarthy.

*Specimens Shown.*

A Specimen Showing Extensive Vegetations on the Pulmonary Valves Alone, from a Case of Malignant Endocarditis, by Dr. D. J. Milton Miller.

A Specimen Showing the Ball-valve Action of a Gallstone in the Common Duct, with a Greatly Dilated Duct and Gall-bladder, and a Multilocular Abscess of the Liver, by Dr. F. A. Packard.

A Specimen of Calcium Phosphate Urinary Calculus, by Dr. Henry M. Fisher.

Specimens from Two Cases of Aortic Disease, by Dr. Joseph Sailer.

Specimen Showing Thrombosis of the Right Innominate, External and Internal Jugular, Subclavian and Axillary Veins from a Case of Aortic and Mitral Disease, by Dr. D. J. Milton Miller.

Specimen of Aneurism of the Arch of the Aorta which Ruptured into the Pericardium, by Dr. J. A. Scott.

Specimen from a Case of Malignant Endocarditis and Brain Abscess, with Unilateral Kernig's Sign, by Dr. Joseph Sailer.

Sample of Green Urine, by Dr. A. A. Eshner

SAMUEL MCC. HAMILL,  
Clerk of Section.



## LIST OF PAPERS: SECTION ON GYNECOLOGY.

*December 20, 1900.*

A Case of Cæsarean Section, by Dr. George M. Boyd.

A Report of Two Cases:

(a) Fulminating Peritonitis.

(b) Carcinoma of the Cæcum, by Dr. R. P. McReynolds (by invitation).

Demonstration of Cystoscope Instruments, with Remarks on Cystitis, by Dr. J. M. Baldy.

*January 17, 1901.*

The Treatment of Prolapsus Uteri, by Dr. E. E. Montgomery.

Cancer of the Cervix and Pelvis Following Supravaginal Hysterectomy, by Dr. C. P. Noble.

Cases of Ovarian Cyst, by Dr. George E. Shoemaker.

*February 21, 1901.*

Varicocele of the Broad Ligament, by Dr. John B. Shober.

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JOHN H. GIRVIN,  
Clerk of Section.



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ON THE  
ALTERATIONS PRODUCED IN THE LARGE INTESTINES OF  
DOGS BY THE AMŒBA COLI, BY HEAT, AND  
BY VARIOUS CHEMIC SUBSTANCES,

WITH NOTES ON THE ANATOMY AND HISTOLOGY OF  
THIS VISCUS.

BY  
H. F. HARRIS, M.D.,  
ATLANTA, GA.

A RESEARCH CARRIED ON UNDER THE AUSPICES  
OF THE NATHAN L. HATFIELD PRIZE COMMITTEE OF THE COLLEGE  
OF PHYSICIANS OF PHILADELPHIA.

---

PHILADELPHIA:  
PRINTED FOR THE COLLEGE.  
1901.

*Es ist immer gut etwas zu wissen.*

GOETHE.

TO  
JUDGE SAMPSON WATKINS HARRIS

AND  
LUCY WATKINS HARRIS,

THIS LITTLE VOLUME  
IS AFFECTIONATELY DEDICATED

BY THEIR SON,

THE  
AUTHOR.

TO

*The Memory of*

NATHAN LEWIS HATFIELD, M.D.,

THIS ESSAY

HONORED BY THE FIRST TRIENNIAL AWARD OF THE

NATHAN LEWIS HATFIELD PRIZE,

IS PUBLISHED BY THE

TRUSTEES OF THE MEMORIAL FUND.

EXTRACT FROM THE MINUTES OF THE STATED MEETING OF THE COLLEGE  
OF PHYSICIANS, HELD MAY 1, 1901.

DR. WILSON moved that the College direct the Trustees of the Nathan Lewis Hatfield Memorial Fund to pay the award of five hundred dollars to DR. H. F. HARRIS, of Atlanta, Georgia, for his research entitled: "A Study of the Alterations Produced in the Large Intestines of Dogs by the Amœba Coli, by Heat, and by various Chemic Substances, with Notes on the Anatomy and Histology of this Viscus."



## PREFACE.

THE experiments, the results of which are recorded in the succeeding pages, were begun in the spring of 1899, in the laboratories of the Jefferson Medical College Hospital, of Philadelphia. During the following summer the work was continued in the Laboratory of Experimental Pathology of the University of Vienna. For permission to work in the latter laboratory the writer is indebted to Geheimrath Prof. Dr. Knoll and to his very able First Assistant, Dr. Biedl, to whom he particularly desires to express his thanks for many kindnesses. In the early spring of the following year the investigations were resumed at the laboratories of the Jefferson Medical College Hospital, where every opportunity was afforded the writer to carry on his experiments by his honored former teacher and colleague, Prof. W. M. L. Coplin, who frequently took upon himself the burden of routine laboratory work, in order that the author might be free to pursue his studies. During the past winter the investigations have been carried on in the Laboratories of Pathology and Bacteriology of the Atlanta College of Physicians and Surgeons. In this connection the writer wishes to express his deep appreciation of the valuable assistance rendered to him, while working in the last-named laboratory, by Dr. C. E. J. Smith and by Mr. Leon Weis, at that time an undergraduate in the Atlanta College of Physicians and Surgeons.



Although during the periods mentioned the writer was almost constantly engaged in this work, it must be confessed that the results appear meagre and disappointing when the few substances experimented with are compared with the vast number of those capable of setting up abnormal processes in animal structures. Notwithstanding this, the author ventures to express the hope that these investigations may be of some value to future laborers in the field of pathologic histology, particularly as they seem to indicate that with the advance in technical methods it will be possible at no distant day to accurately determine the nature of all disease-producing causes by the character of the lesions induced in the tissues.

MARCH, 1901.

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PART I.  
TECHNICAL METHODS.





## PART I.

### TECHNICAL METHODS.

It has very often occurred that investigators in recording their experiments have failed to state in a distinct and clear manner the technical methods employed by them, and as a consequence subsequent observers have not infrequently failed, either wholly or in part, to corroborate their results. For this reason it appears to the writer that a brief résumé of the methods employed by him during the course of his work will not be without value.

Great care was always exercised to avoid causing unnecessary pain to the dogs experimented upon. Shortly before the use of any of the irritating substances that were administered to them the animals were invariably given a large hypodermatic injection of morphine, and in all instances where operative procedures were required, or where an unusual amount of pain would have resulted from the manipulations, ether was in addition exhibited. After the experiments were finished, if the animal did not die as a result, chloroform was given until death was produced. In all instances the animal was instantly opened following death, but in a few cases where the dogs died during the night a post-mortem examination was not made until the following morning. With great care, and always avoiding pressure or force of any kind upon the walls, the large bowel was removed, and without coming in contact with any fluid, or other substance, was immediately placed in a fixing solution. At the time of the beginning of these investigations numerous experiments were made to determine the best method of keeping the wall of the bowel stretched during the time that it was kept in the fixative, and in the subsequent alcoholic solutions, as it was found that as soon as the specimens were

immersed the muscular structures contained within them always contracted and caused great distortion. After numerous trials the following plan was adopted: As soon as the intestine was cut open one of its ends was pinned to a thin piece of board by means of tacks, and then grasping the other end of the bowel the walls were stretched to a moderate degree; tacks were then fastened along and around its edges at whatever points were necessary to hold it in this position. It is, of course, true that the tissues in the immediate neighborhood of the tacks are not suitable for microscopic examination, but with a little care there was no difficulty in so placing them that the most interesting portions of the lesions were entirely unaffected.

At first a large number of different fixing solutions were tried, to enumerate all of which would be entirely profitless; suffice it to say that excellent results were gotten by the use of both Fleming's and Hermann's solutions, and also by the use of corrosive sublimate alone, and the various mixtures containing it. However, after much investigation the corrosive sublimate mixture of Bensley, employed by him for the study of the prozymogen granules in the cat's stomach, was found to be most generally applicable. The reasons for this selection are that while the osmic mixtures just referred to preserve the morphologic constituents of cells most admirably, it is impossible to obtain after their use some of the microchemic reactions of the granules of certain cells, and none of the other corrosive sublimate mixtures preserve the structure of the cells, and at the same time permit their chemic investigation so well as the mixture selected. Bensley's solution is made as follows:

One to two per cent. bichromate of potassium in water.

Saturate solution of corrosive sublimate in alcohol.

Equal parts of these two solutions are mixed together just before use, and the tissue is immersed in the mixture for from one-half to two hours. The tissues are next washed well in water, dehydrated, cleared, and embedded in paraffine in the usual way. When using large blocks of paraffine the writer has found that this substance does not harden properly when cooled rapidly, as is generally recommended, but that it assumes most excellent cutting consist-

ency if kept at about 37° C. for a day or two. Sections are then cut; for this purpose the Minot-Blake microtome has recently been used, and with a sharp knife it certainly produces the most even and uniform sections that the writer has ever seen. After being cut the sections are spread and fastened to the slides by Ohlmacher's method; they are then thoroughly dried, the paraffine is dissolved off with xylol, the corrosive sublimate crystals are removed with tincture of iodine, and the sections are soaked in pure alcohol until the iodine is entirely removed. They are then ready for staining. The numerous solutions through which the sections were carried were kept in the staining jars devised by Coplin, which are so convenient that the writer thinks special mention should be made of them.

For the purpose of staining nearly all of the usual methods, and quite a number of special ones, were employed from time to time, but in every instance a greater or less number of sections were prepared by the following methods:

In order to obtain a general idea as to the state of the tissues, specimens were always first stained with hæmatein, the writer's solution of which is prepared as follows:

Hæmatoxylin . . . . .	1 gm.
Alcohol . . . . .	10 c.c.

The former is dissolved in the latter, and 500 c.c. of a saturated solution of alum in water is added. Boil, and while in this state add 0.5 gm. of mercuric oxide. In a few moments the solution turns to a dark, rich purple color, and the vessel containing it is then removed and cooled rapidly. After cooling the solution is filtered, and 4 per cent. of glacial acetic acid is added. This mixture keeps excellently, and although much cheaper it is in every particular equal to Mayer's acid hæmalum. The stain may be used in the concentrated form, but it is preferable to employ it greatly diluted with water, or, perhaps better, with an aqueous solution of alum, and to allow the section to remain in it overnight. In this way an almost pure nuclear stain is obtained, and one which can scarcely be surpassed by any of the coal-tar colors.

In many instances the specimens were counterstained with eosin after previous treatment in the hæmatein stain. The solution of eosin that the writer has constantly employed for a

number of years is prepared by adding alcohol-soluble eosin and water-soluble eosin (the latter is also soluble in alcohol) to ordinary 95 per cent. alcohol to the point of saturation. It has been found that with a solution prepared in this way many of the morphologic elements of tissues may be readily differentiated from each other—as, for example, muscle and fibrous tissues are stained in such different tones of red that they may be told apart at a glance.

Picric acid is also an excellent counterstain for hæmatein; it makes the tissues look clearer than any other plasma stain.

For the purpose of especially studying the mitotic figures that are so abundant in the deeper portions of Lieberkuehn's crypts, and also for investigating the other nucleated structures in the tissues, Benda's hæmatoxylin method was found to be most serviceable. Counterstains may be also employed after sections have been colored in this way, but inasmuch as the stain is itself a most excellent one for the plasmatic structures of cells, this is generally unnecessary.

For the purpose of studying fibrous tissue there is perhaps no method that is altogether so satisfactory as Van Gieson's. Instead of Delafield's hæmatoxylin the writer always uses the acid hæmatein, to which reference has already been made; the latter solution is preferable, as the nuclei are alone stained by it. In tissues prepared in this way the connective tissue fibrils appear under the microscope with diagrammatic clearness, and the other structures are also well shown.

In all of these investigations it has been of great importance to determine the extent of the formation of mucin in the glands, and, thanks to that most eminent technologist, Mayer, we possess in his muchæmatein a most admirable reagent for the demonstration of this substance. This stain may be prepared directly from hæmatein, as was recommended by Mayer, but the solution devised by the writer is in every way as efficient, and much less expensive. It is made as follows:

Hæmatoxylin . . . . .	0.2 gm.
Aluminium chloride . . . . .	0.1 "
Glycerin . . . . .	50 c.c.
Water . . . . .	50 "

Mix and dissolve the first two ingredients in the last. Boil. While boiling add 0.2 gm. of mercuric oxide. The mixture very quickly assumes a dark purple color. It is then cooled and filtered. This stain may be employed in a concentrated form, or water may be added to it very largely before it is used. The mucin assumes almost exactly the same color as the staining solution—*i. e.*, it presents after treatment a beautiful rich purple hue; with the exception of the granules found in mucinoblasts no other structures found in the dog's intestine are tinted in this way by the stain.

One of the most useful combinations of these stains consists in treating sections with the hæmatein solution first, then washing off with water, staining next in muchæmatein, and after passing through water and alcohol finally counterstaining in an alcoholic solution of picric acid. When tissues are prepared in this way the nuclei have a dark brownish color, the mucin appears of a bright purple hue, and the surrounding protoplasmic structures are dyed in varying tones of yellow. Perhaps in no other way can such a general conception of the state of the entire intestinal wall be gained so clearly and so quickly as from an examination after the tissues have been stained in this way.

Inasmuch as the intestinal wall contains considerable quantities of elastic tissue, it was necessary in all instances to differentiate these structures in such a way that their condition might be properly examined into. In order to do this Weigert's stain for elastic tissue was in the beginning always employed, but later the following method was used:

During these investigations a series of accidents led the writer to discover the fact that hæmatein solutions, when prepared in a certain way, have a remarkable affinity for elastin, and that this substance may be differentiated clearly from other tissues by the employment of the peculiar stain in question; and, inasmuch as the results obtained by its use appear to be in some particulars superior to those gotten from Weigert's method, the former has been recently usually substituted for the latter. The stain is made in the following manner:

Hæmatoxylin . . . . .	0.2 gm.
Aluminium chloride . . . . .	0.1 "
Fifty per cent. alcohol . . . . .	100 c.c.

Dissolve the hamatoxylin and aluminium chloride, and then carefully bring the solution to a boil; 0.6 gm. of mercuric oxide is now slowly added, and as soon as the mixture assumes a dark purple color it is removed from the flame and cooled rapidly. The stain is filtered, and one drop of hydrochloric acid is added. A short time after cooling a flocculent precipitant is sometimes formed in the solution; this is immediately dissolved upon the addition of the hydrochloric acid. The stain should then be set aside for some weeks, as it will not, as a rule, give satisfactory results at once.

The writer has not been able to find the reason for this, but the change does not appear to depend upon the continued absorption of oxygen by the hamatein, for the reason that no degree of artificial oxidation seems to quicken the result. It must be admitted that this stain is somewhat capricious in its "ripening," but after this has been once accomplished it appears to keep indefinitely. The stain is used by immersing thin sections of tissue in it for from five to ten minutes, and then washing off for about a minute in a 1 per cent. solution of nitric acid in alcohol; the acid alcohol is then thoroughly removed with pure alcohol, and the sections are cleared and mounted. The elastic tissue fibrils are stained a uniform dark purple hue, while the other tissues are colored in varying tones of red. This method seems to offer an advantage over that of Weigert, in that there is not so much tendency to color the neighboring fibrils of collagenous tissue, and that even in those cases where this does occur the tint is entirely different. This stain is so closely related chemically to Mayer's muchematein that the name *clasharmatein* naturally suggests itself for it. It may be of interest in this connection to remark that when tissues are treated with Mayer's mucicarmine and afterward with an alcoholic solution of nitric acid, any elastin that may be present stains much more brilliantly than do the other structures, and this method, as a consequence, may be used for differentiating between them. With both of these stains mucin is always decidedly colored, but inasmuch as this substance is rarely found in those localities where elastic tissue occurs, and is morphologically entirely unlike it, there is no possibility of confusing them.

Of all the methods for the demonstration of mucinoblasts<sup>1</sup> and plasma cells there is none which is, perhaps, so available for general work as the writer's carbol toluidin-blue, the reasons for this being that the stain is perfectly permanent, and, on account of its neutral reaction, does not injure the delicate nuclear network of cells. This stain is prepared by dissolving from 1 to 2 per cent. of toluidin-blue in a 2 to 4 per cent. solution of carbohc acid in water. Sections may be stained for from a half-minute to several days. Before and after staining the tissues should be always washed thoroughly in water, as this prevents the precipitation of particles of the dye that invariably occurs when the stain is brought directly in contact with alcohol. After washing the sections may be differentiated, especially if thin, in ordinary alcohol, cleared in xylol or cedar-wood oil, and mounted in the usual way, or this result may be, perhaps, better accomplished by treating them with Unna's glycerin-ether mixture diluted from five to ten times with water; in from five to ten minutes the process is completed and the section is then quickly washed in alcohol, cleared in cedar-wood oil or xylol, and mounted in balsam. In this way the granules in the mucinoblasts are colored red, while the finer particles lying in the protoplasm of the plasma cells assume a dark bluish color. This reaction is evidently due to differences in the chemie nature of the granules of these cells, and not, as Unna stated when speaking of his alkaline methylene-blue solution, to the presence of different coloring agents in the stain. It should here be said that the glycerin mixture of Unna above referred to cannot be prepared very conveniently without the apparatus which is usually only found in a chemie laboratory, and that the mixture had best be purchased from Gruebler, or from some of the microscopic dealers in this country who supply his reagents.

In many instances, especially where necrotic changes are in progress, it becomes of much importance to determine if the

<sup>1</sup> The word "mucinoblast" is constantly employed in this essay in describing those peculiar cells to which Ehrlich gave the name of mast cells. If we may rely on microchemie reactions the granules in these cells consist of mucin, as the writer has shown in another place, and the former name therefore appears much more appropriate than the latter.



tissues react to dyes in the usual way—*i. e.*, if those structures that normally take the basic stain and those that are colored in health by acid dyes still retain these peculiarities in a normal manner; this important point can be determined in no better way, nor more clearly, than by staining the sections for from a few minutes to several hours in the carbol toluidin-blue solution already referred to, afterward washing off with water, then quickly in alcohol, and finally immersing the tissues for a few seconds in the alcoholic solution of both water- and alcohol-soluble eosin, to which reference has been made. After the treatment in this way the section is again rinsed in alcohol, cleared in xylol or cedar-wood oil, and finally mounted in balsam. All those structures that have affinity for basic dyes are stained blue, while the eosin colors the remaining tissues in varying tones of yellowish-red. It is of importance in all cases that the eosin solution should be an alcoholic one, as it does not abstract the basic dye so readily, and, in addition, produces in the tissues differential effects that are never obtained when the stain is applied dissolved in water.

Fibrin has been sought for by staining the tissues with aniline gentian violet in the way recommended by Weigert. In carrying out the process the usual steps have been followed, but it may be mentioned that the writer has found that the staining solution may be preserved indefinitely by adding to it from 1 to 2 per cent. of tincture of iodine in which a small quantity of corrosive sublimate has been dissolved. It is quite possible, though it has not been tried, that an alcoholic solution of iodide of mercury, or even of corrosive sublimate, would accomplish the same result.

PART II.

ANATOMY AND HISTOLOGY OF THE LARGE INTESTINE  
OF THE DOG.



## PART II.

### ANATOMY AND HISTOLOGY OF THE LARGE INTESTINE OF THE DOG.

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AT the time when the writer of this essay began his experiments on the large intestines of dogs a thorough search was made of all available literature on the subject of the anatomy and histology of the viscus upon which the investigations were to be conducted. This examination of the literature revealed the fact that the histologic descriptions that have been heretofore given of the dog's large intestine are of a most meagre character, and, indeed, on account of the lack of proper methods, until within the last few years there were some details concerning which accurate observations could not have been made. During the course of his studies the writer has found structures in the coats of the intestines of these animals of which he has been unable to find any description, and, in addition to this, he has been led to conclusions concerning the method of the formation of mucin that are new, so far as he is aware, and if on further investigation they should be found true, cannot fail to be of value in elucidating the method of the formation of this substance in man and in other animals. For these reasons it has been thought not unwise to give a description of the anatomic and histologic appearances of the intestine before beginning the consideration of the alterations that may be artificially produced in the tissues composing it.

The large intestine of the dog cannot, as in the human being, be properly divided off into several different parts. Beginning at the anus the intestine proceeds forward in an almost straight line until within 5 or 6 cm. of its termination, where it curves toward the right side of the animal's body and becomes united

to the small intestine only a short distance behind the liver; it would thus appear that the greater part of the viscus might not inappropriately be styled the rectum—using the word in its generic sense. Its length and breadth vary, depending upon the size of the animal in which it occurs, but in the average dog it is 25 to 30 cm. in length. Its circumference also varies, depending upon the size of the animal and upon whether or not its muscular walls are in a state of contraction; in an ordinary dog this measurement will perhaps average from 5 to 7 cm. The intestine is attached to the upper portion of the wall of the abdomen by a mesocolon which very closely resembles that found in man. The wall of the bowel varies considerably in thickness, this again depending upon the size of the animal and also upon the state of contraction of its muscular layers; when in a relaxed condition and when normal it is, as a rule, about 3 mm. in thickness; but if it be contracted, or in a diseased state, this measurement may be doubled. The mucosa of the normal intestine is soft and velvety and of a pinkish-gray color; its surface is not, as a rule, smooth, the mucosa presenting numerous elevations and depressions, the number and size of which entirely depend upon the state of contraction of the muscular layers. These elevations, or rugæ, especially in the upper portion of the bowel, are occasionally longitudinal with its course, but in the lower half of the gut, particularly when the viscus is inflamed, they are almost always nearly or quite transverse to its long axis.

Examination with a low power shows the wall of the bowel to be divided into layers quite similar to those found in the intestine of man. These consist of a *mucosa*, a *muscularis mucosæ*, a *submucosa*, a *circular* and a *longitudinal muscular layer*, a *subserous coat*, and a *serous coat*, a detailed description of which now follows:

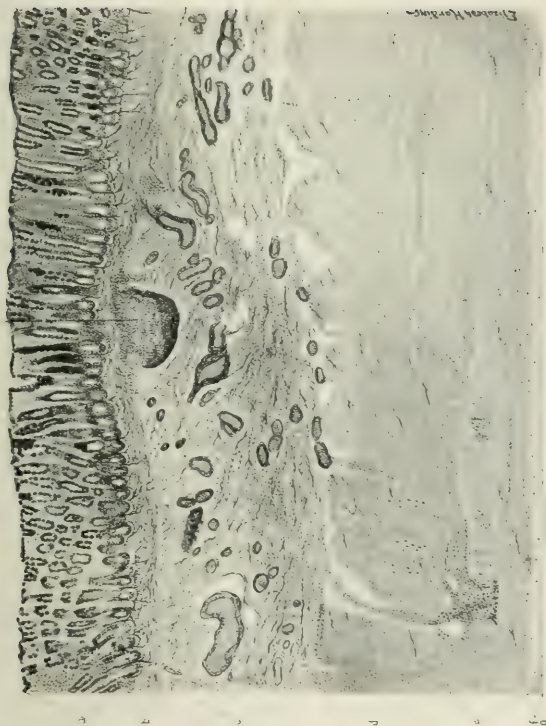
The *mucosa* has in the adult dog a thickness of about 1 mm. When examined under the microscope this coat is not uncommonly found covered with a thin layer of mucus, in which there are usually particles of undigested food, fragments of desquamated epithelial cells and bacteria; this layer varies very much in thickness, sometimes being entirely absent. Covering the surface of the mucosa there is a single layer of epithelial cells; these cells

vary in height from 14 to 20 $\mu$ , with an average of about 18 $\mu$ . They vary exceedingly in width and are very irregular in form. In instances where they contain mucin they are commonly barrel-shaped, while the cells lying in the vicinity are constricted in the middle, thus resembling in their form the spools upon which thread is wound; not uncommonly they are columnar in form, while in other instances they are wedge-shaped. It is thus apparent that it would be impossible to state with any degree of accuracy their average width, and even the same cell always varies in this measurement in its different parts. The largest of all these cells are those that contain mucin, the width of which is sometimes as much as 20 $\mu$ . Near the basal portion of the cells there is always a single vesicular nucleus, which may be rounded, oval in form, or spindle-shaped; the nucleus is surrounded by a distinct nuclear membrane, on the inner edge of which there are from five to eight minute masses of chromatin that vary considerably in size, and in the central portions of these nuclei a nucleolus is usually encountered. These nuclei vary in diameter from 4 to 8 $\mu$ . The protoplasm of the cells is finely granular and stains with acid dyes. Mucin formation is very commonly observed in these cells; in the beginning the protoplasm of the cell becomes paler just above the nucleus, and on staining with the proper dyes this region is found to contain mucin. If specimens be stained lightly with Mayer's muchæmatein, or by the toluidin-blue picric acid method, there are found within these areas small, rounded, oblong or irregularly shaped masses which take the stain much more deeply than the surrounding mucin, and under these circumstances investigation will not uncommonly reveal a mucinoblast lying flattened out over the basement membrane to which the cell is attached. These masses resemble very greatly in form and in their staining reactions the granules encountered within the mucinoblasts. In a number of instances close investigation revealed the presence of granules lying in the protoplasm of the cells, between the mucinoblasts and the area containing mucin; it would thus appear that they have penetrated the basement membrane and have passed into the protoplasm of the mucin-bearing cells. The suggestion is therefore made that the mucin as it is found in the epithelial cells may have its origin, in part, in the

granules that are contained within the mucinoblasts, and that these pass through the basement membrane upon which the epithelial cells lie, penetrate the protoplasm of the cells, and there, probably becoming united with some of the cellular constituents, produce what we call mucin. As the mucin-bearing cell increases in size these small masses become more numerous, and there appears to be little doubt—whatever their origin may be—that they exercise an important function in the production of mucin. As the mucin forms the cells increase in size, and, while they not uncommonly become somewhat longer, the enlargement occurs to a much greater extent in a lateral direction, with the result that they ultimately become rounded in form. Under these circumstances the protoplasm of the cell seems almost entirely to disappear, and the nucleus, reduced much in size and compressed into a crescentic form, lies between the masses of mucin and some part of the basal wall of the cell. The outline of the cell under these circumstances is by no means distinct, and the writer has in no instance been able to definitely determine whether the mucin remains confined to the original cell in which it begins, or whether it bursts into the surrounding cells; although this view would appear not impossible, it seems probable that this does not happen, for the reason that the mass of mucin would scarcely, under these circumstances, assume a rounded form and that there would be distinctly present beneath the masses more than one nucleus, which the writer has never been able to observe. In properly stained specimens the mucin may be frequently found in the act of discharging itself into the lumen of the intestine, but the writer has never been able to determine the subsequent fate of the remaining portion of the cells under these circumstances.

The surface of the intestine is beset with countless numbers of minute depressions which are the openings of those long, cup-shaped glands known as the *crypts of Lieberkuhn*. These structures are of two kinds—the *surface crypts* and those that, from their situation, the writer has called *lymph node crypts*; the latter correspond to the lacuna that have been described in the small intestines of some of the lower animals. The epithelial cells covering the surface of the intestine become continuous with those that line these glands, to which they are in almost every way similar.





Section from about the middle portion of the large intestine of a dog. Specimen fixed in Bessley's solution. The drawing is a composite one, having been made from a section stained with hemalum, muciachrom, and picric acid, and another stained with elashamatin. Each  $\frac{1}{2}$  inch. Oc, 1 inch. *a*, Mucosa. *b*, Muscularis mucosa. *c*, Submucosa. *d*, Circular muscular layer. *e*, Longitudinal muscular layer. *f*, Subserous coat, showing elastic tissue basement membrane. *h*, Bands of elastic tissue. *i*, Lymph node. *j*, Bloodvessels, in the walls of which there is much elastic tissue.



The *surface crypts* are almost as long as the mucosa is deep, there being between their bases and the muscularis mucosæ a distance of only about  $30\mu$ ; from basement membrane to basement membrane they vary from 60 to  $75\mu$  in diameter, with an average of perhaps about  $65\mu$ . They may be divided into four portions—a *mouth*, a *neck*, a *body*, and a *base*.

Where the crypt opens upon the surface of the intestine there is a funnel-shaped depression—the *mouth* of the crypt. In this situation the epithelial cells lining the parts present peculiarities similar to those that characterize the surface layer of cells, with the exception only that mucin formation goes on here to a somewhat greater degree.

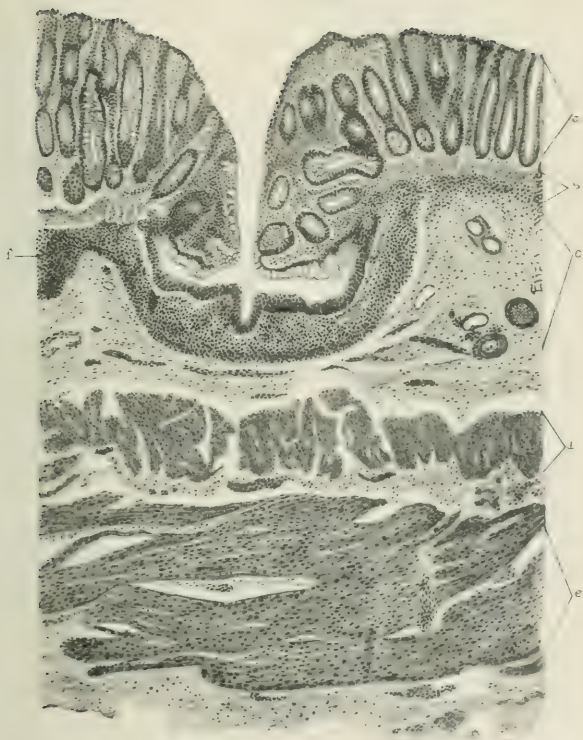
Immediately beneath the mouth of the crypt, and continuous with it, is the *neck* of the gland. Here the epithelial cells suddenly become considerably longer, this being in a large measure the result of the presence of great numbers of mucin-bearing cells. As a result of this the lumen of the crypt is suddenly greatly decreased in diameter.

Beneath the neck of the gland comes its *body*, which comprises practically the entire lower two-thirds of the crypt. In the upper portion of the body of the gland the epithelial cells are in every way similar to those found in the necks of the glands, but as the basal portion of the structure is approached they gradually become shorter as a result of the fact that mucin formation occurs with less and less frequency.

At the base of the crypt the epithelial cells become even shorter still, and, as a rule, the lumen of the crypt rather abruptly enlarges, it being here from 30 to  $35\mu$  in diameter. The epithelial cells in this situation are generally from 12 to  $18\mu$  in height, and the basal portion of their protoplasm contains multitudes of minute basophilic granules, causing them to appear when stained much darker than the cells higher up. These granules contain iron; it is highly probable that they are closely associated with the production of some substance that assists in the process of digestion, as they are nearly related to the prozymogen granules described by Bensley in the cells of the gastric tubules, and by Macallum in those of the pancreas. It is further true that mucin formation very rarely occurs in these cells in health.

In addition to the minute openings on the surface constituting the mouths of the surface crypts there are here and there found larger and much deeper depressions, these being the channels that communicate with the *lymph node crypts*. On examination it is found that the entire mucosa dips downward into the submucosa in these situations, and that that part of the mucosa that lies at a lower level than the muscularis mucosae is entirely surrounded by masses of lymphoid tissue. The glands that open around the edges of the mouths of the lymph node crypts resemble in every way those present in other situations, but just at the bottom of the crater-like depression there are always found one or more crypts that differ somewhat from those higher up. These glands are characterized by the fact that from the bottom of the large opening there radiate at right angles numerous primary glands, and these in some instances give off branches. These glands are further peculiar in that they are very large, some of them being from basement membrane to basement membrane as much as  $140\mu$  in diameter. The cells lining the openings leading into these crypts resemble in every way those that are found in the necks of the surface glands, and, like them, oftentimes contain mucin, —this peculiarity, curiously enough, being particularly prominent on the sides of the ducts toward the free surface of the intestine. The mucin-bearing cells in these situations are the tallest epithelial cells found in the large intestine of the dog, they being commonly from 40 to  $50\mu$  in height. In the deeper portion of these crypts the epithelial cells resemble in every particular those found in the bases of the surface glands, with the exception only that they are generally considerably larger, usually measuring from 25 to  $30\mu$  in height. These cells do not lie on a basement membrane, but seem to be in direct contact with the lymphoid cells that are immediately beneath them; this peculiarity of the cells in these situations has been noted in the intestines of other animals by Davidoff, and this portion of the gland was called by him the *intermediary zone*. The epithelial cells lining the deeper portions of these glands, as well as those occurring in like situations in the surface crypts, often contain mitoses; they are easily found, for the reason that nuclei undergoing this change lie more superficially than those in the resting stage.

PLATE II.



Specimen from the upper portion of the large intestine of a dog. Specimen fixed in Bensley's solution and stained with haemalum and eosin. Beck  $\frac{1}{4}$  inch. Oc. 1 inch. *a.* Mucosa. *b.* Muscularis mucosæ. *c.* Submucosa. *d.* Circular muscular layer. *e.* Longitudinal muscular layer. *f.* Lymph node. *g.* Lymph node gland.



The cells lining the crypts of Lieberkuehn lie upon a delicate basement membrane which is thickest around the basal portion of the glands, and becomes at the mouths of the crypts, and beneath the epithelium lining the superficial surface of the mucosa, exceedingly thin. Around the bodies and bases of the glands this membrane has an average thickness of about  $2\mu$ , but beneath the surface epithelium it generally measures something less than  $1\mu$  in thickness. It is very interesting to note that this membrane reacts in a perfectly characteristic manner to the elastic tissue stain of Weigert, and to the hæmatein elastin stain described in Part I.

Between the crypts there is always a certain amount of interglandular substance, varying in thickness from 5 to  $15\mu$ . This contains a delicate network of fibrils of what appears to be collagenous tissue, since they react perfectly to the stains that exhibit most affinity for this substance. These fibres commonly measure something less than  $1\mu$  in thickness. Lying in the lymph spaces between the collagenous tissue network there are always found quite a number of lymphoid cells, an occasional polymorphonuclear leucocyte, quite a number of mucinoblasts, and, in addition, especially around the bases of the glands, there are commonly present cells that have the shape of and stain very much like plasma cells. The mucinoblasts commonly lie in contact with the basement membranes of the crypts, upon which they seem to be flattened out; reference has already been made to the fact that the granules found in these cells appear in some instances to permeate the basement membranes and to penetrate the mucin-bearing epithelial cells. The cells above mentioned that so closely resemble plasma cells differ from them only in that the granules that they contain are, as a rule, not altogether so large and do not take the basic stain with precisely the same degree of intensity as the granules found in these cells. Minute capillaries are frequently found in the interglandular tissues. The structures that lie between the bases of the crypts and the muscularis mucosæ resemble those occurring between the glands in every particular, with the exception only that the pseudoplasma cells are more commonly present, and that there pass up through it many fibrils of elastic tissue from the muscularis



mucosa. These bands of elastin become united to the outer portions of the basement membrane of the crypts at the points where these structures pass upward to surround the bodies of the glands, and they are of great importance, as they afford the only real attachment of any strength that binds the mucosa to the layers underneath.

The *muscularis mucosa* is composed of two parts—an inner circular and an outer longitudinal muscular layer. In some situations the outer longitudinal layer becomes exceedingly thin, and may for a short distance entirely disappear. In those areas where the lymph node crypts exist the entire muscularis mucosae is interrupted, no vestige of it being found in the surrounding tissues. The muscularis varies considerably in thickness, but the two coats together are perhaps, on an average, of about  $75\mu$  in thickness. It is very curiously the case that the longitudinal layer in those situations where it occurs is usually somewhat thicker than the more constant inner circular layer, the former measuring usually about  $45\mu$  and the latter  $30\mu$  in thickness. These layers are largely made up of ordinary unstriped muscle fibres which contain about their central portions spindle-shaped nuclei. It was impossible to measure the length of these fibres with any accuracy in sections, and for this reason no attempt will be made to give their dimensions further than to say that they appear to be about the usual size of unstriped muscular fibres.

Between the muscular tissue there is a delicate network of elastic tissue, the fibrils measuring from 1 to  $2\mu$  in thickness. These fibres become continuous with those that pass up through the tissues lying beneath the bases of the crypts, and, as before stated, ultimately attach themselves to the outer portions of the basement membranes that surround the bodies of the glands.

Beneath the muscularis mucosa, and separating it from the circular muscular layer, is the *submucosa*. This coat has an average thickness of perhaps 0.5 mm., but it varies considerably in this measurement. The coat is always much thicker immediately beneath those elevations on the mucous surface that have been described in speaking of the anatomy of the intestine, but it is highly probable that these rugae are never constant in any one situation, and that the increased thickness of the submucosa is

only of a temporary nature. These puckerings of the submucosa are unquestionably due to contractions of the muscularis mucosae. The submucosa is made up almost entirely of collagenous tissue, mixed with which there is more or less elastin; although the fibrils composing these tissues run, for the most part, in a circular manner, many of them run longitudinally and some obliquely. Lying within the tissues there are quite a number of fixed connective tissue cells and many mucinoblasts; in addition to these an occasional lymphoid cell or polymorphonuclear leucocyte may be found. Scattered all through the tissues there are numerous bloodvessels. The submucosa of the large intestine of the dog is particularly rich in lymph nodes, these being in some cases so small that they do not occupy more than one-fifth or one-sixth of the thickness of the gut, while in other instances they replace the tissues completely from the circular muscular coat to the surface epithelium that covers the mucosa. In the larger nodes there are frequently present those peculiar lymph node crypts, a description of which has already been given. These lymph nodes are made up of lymphoid cells almost entirely, but there are not uncommonly in addition a few pseudoplasma cells, and an occasional mucinoblast. No lymphatics penetrate these structures, but there are always a number of vessels of this kind surrounding the nodes. This coat also contains nerve plexuses, in which there are medullated and non-medullated nerve fibres and likewise ganglion cells.

Immediately external to the submucosa is the *circular muscular layer*, to which it is united by numerous prolongations of the former that pass down between the bands of muscle fibres, forming the intermuscular septa. The thickness of this layer varies somewhat, depending upon the state of contraction of the fibres composing it, but in general it is from 1 to 1.25 mm. in thickness. In addition to the intermuscular septa just referred to, the coat is made up of unstriped muscle fibres that correspond in every way to those referred to as occurring in the muscularis mucosae. Between the muscle fibres everywhere there is a delicate network of elastic tissue. This network is composed of comparatively coarse fibres that radiate from the intermuscular septa; the fibrils measure from 0.5 to 1 $\mu$  in thickness. These structures stain intensely

with the specific stains for elastic tissue, and there can be no question of their true nature. Radiating from these large bands there are multitudes of minute fibres, having a diameter of from  $0.3$  to  $0.4\mu$ , that lie between each individual muscle fibre and act as sheaths for them. It should be noted that elastic tissue is very abundant in the intermuscular septa. In the lymph spaces of the muscular layers there are generally present quite a number of mucinoblasts and lymphoid cells, and polymorphonuclear leucocytes are occasionally encountered.

External to the circular muscular layer is the *longitudinal muscular layer*; this coat is united to the circular muscular layer by means of bands of collagenous and elastic tissue, each being present in about equal quantity. The longitudinal muscular layer is somewhat thinner than the circular muscular layer; but in some situations, as, for example, at the point where the mesocolon is attached, this layer even becomes much thicker. The histology of this coat corresponds in every way to that of the circular muscular layer.

External to the longitudinal muscular layer there is a thin coat composed of a loose network of fibrous and elastic tissue that is very variable in thickness and in its component parts; this is the *subserous layer*. It contains, in addition to bloodvessels, nerves, and lymphatics, quite an amount of fat where the mesocolon is attached. There are occasionally found in its tissues a few connective tissue cells and an occasional lymphoid cell or polymorphonuclear leucocyte.

At all points, except where the mesocolon is attached, the subserous coat is covered by a *serous layer*. This is made up of delicate basement membrane that gives an intense stain-reaction to the specific stains for elastic tissue. The membrane is covered on its external surface by pavement epithelium, upon the free surface of which, in properly prepared sections, minute cilia may be demonstrated.

PART III.

EXPERIMENTAL DYSENTERY IN DOGS.



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### EXPERIMENTAL DYSENTERY IN DOGS.

NUMEROUS attempts have been made by the writer to experimentally induce changes in the intestines of dogs by the rectal injection of various bacteria and fecal matter from individuals suffering from dysentery. Among the organisms experimented with are the so-called typhoid bacilli, colon bacilli, the ray-fungi, anthrax bacilli, the staphylococci and streptococci of suppuration, the mixed bacteria that were grown from the feces of individuals suffering with dysentery, and the so-called bacillus dysenteriae of Shiga. As a general rule, several dogs have been experimented upon with each of the organisms mentioned; in a number of cases they were quite young, and therefore presumably somewhat more susceptible than older animals. In order to prevent the injected material from being at once expelled, in almost every instance the dogs received morphine hypodermatically an hour or so before the bacteria were introduced into their intestines, and there can be no doubt that in practically all cases the micro-organisms were retained in sufficient quantity to furnish a reasonable test of their pathogenic power. Bouillon cultures of the bacteria were in most instances used for the experiments, though in some cases the organisms were removed in mass from solid media and thoroughly ground up with sterilized water in a mortar before being injected. As a general rule, 10 c.c. of the bouillon cultures were administered, but in some cases the amount was greater and in some less. A record of the time, the quantity of bacteria injected, and the sizes of the dogs experimented upon was carefully kept in every instance, and the subsequent histories of the animals were likewise preserved. A study of these records shows that not in

a single instance did a dog exhibit evidences of disease following the injection of bacteria, and in most cases they were entirely healthy for weeks and even months thereafter. These results are of much interest, particularly as regards the organism supposed to be the cause of the acute dysentery of the East—the bacillus first described by Shiga. The cultures used were obtained from Prof. Simon Flexner, of the University of Pennsylvania, to whom the writer desires to express his thanks. It seems significant that these organisms entirely failed to produce any effect on four ten-day-old puppies, into the large intestines of which they were injected, nor did any disturbance follow when they were introduced into the large intestines of three cats.

Much more satisfactory were the results obtained by injecting fresh feces of individuals suffering with dysentery into the large intestines of puppies, for in every case in which this was done a typical dysentery immediately developed that resulted in the death of the animals, except in one instance where the dog was killed. It should, however, be stated that no ill effects followed the injection of material of this kind into the large intestines of four adult dogs and in three cats that were almost grown. It would thus seem that puppies are particularly susceptible to the disease-producing cause of this variety of dysentery. These are not the first successful experiments of this kind, for Ilava<sup>1</sup> induced dysentery in two dogs out of seventeen injected with dysenteric material, and in four cats out of six that had been subjected to a like treatment. Kartulis<sup>2</sup> succeeded in producing dysentery in three cats out of seven, he having injected the stools from patients suffering with dysentery, and also cultures of the amoebæ.

Numerous attempts were made to cultivate the amoebæ, but in no instance were they successful; it was therefore impossible to determine what the result would be should these micro-organisms be introduced in this state into the intestines of animals; but the experiments of Kartulis, already referred to, indicate that the pathogenic agency exists in cultures containing amoebæ made from the discharges of patients suffering with dysentery, and he even

<sup>1</sup> Centralbl. f. Bak., Band i., 1887.

<sup>2</sup> Einiges über die Pathogenes der Dysenteriaemoeben, Centralbl. f. Bak., ix., 1901.



asserts that the disease was produced in a cat as a result of the introduction of these organisms in a pure form into its intestine. There seems, however, some tendency among writers to doubt the correctness of his statements concerning the latter experiment, for the reason that no one else has so far succeeded in obtaining these parasites in pure culture.

Since it was impossible to cultivate the amoebae, it occurred to the writer that the next best thing would be to attempt to cultivate all of the bacteria in the discharges of dysenteric patients, and to determine if these mixed cultures were capable of setting up a dysenteric process. Cultures were accordingly made from the feces of the same individuals whose discharges had been used to successfully produce dysentery, and these were then injected into the intestines of four puppies. There was absolutely no effect produced. It therefore seems unreasonable to conclude that the germ that produces the disease is a bacterium, or, at any rate, it seems fairly certain that it cannot be an organism that develops or even lives in the culture media ordinarily employed. As neither of these suppositions appear at all probable, and as the amoeba coli was the only other living organism found in the feces that was probably absent from the cultures, it seems logical to suppose that this parasite is the cause of any morbid state that the injection of these discharges may give rise to. As will be seen further on, this view is supported by the fact that the amoebae are abundantly present in and around the ulcers that are found in the intestines of the dogs suffering with experimental dysentery, and it does not appear unreasonable to say that the proof is now fairly clear that these organisms are in reality the causative agents in chronic dysentery.

### **Dysentery in Dogs Resulting from the Injection of the Discharges of Individuals Suffering from Dysentery.**

#### **EXPERIMENT I. Duration, about four days.**

On December 7, 1900, at 5 P. M., about 0.5 c.c. of fresh fecal matter, from a negro woman suffering with dysentery, was injected into the large intestine of a puppy three days old. Some

of the fecal matter examined immediately before the injection was given showed that it was made up very largely of mucus, mixed with blood, in which there were many bacteria and a large number of living amœbæ. The animal was not examined until four days later, when there was found quite a quantity of slightly blood-stained mucus around the anus and in its immediate neighborhood. Two of the puppies of the same litter that had been simultaneously injected with the dysenteric material also showed blood-stained mucus around their anuses, but five others that had not been injected presented no evidence of the disease. Some of the mucus from each of the puppies was immediately submitted to microscopic examination, and in every instance found to contain many active amœbæ, numerous blood cells, and a great number of bacteria.

The puppy first referred to was killed and a post-mortem was at once made. About one-fourth of the large intestine, from the anus upward, was greatly swollen; its mucous surface appeared rough and uneven, and was of a grayish color, with here and there minute pinkish spots upon it. On close inspection it was evident that the irregularities just referred to were the result of superficial necrosis of the mucous membrane, and that shallow ulcers had already begun to form on the surface of the intestine.

Sections of the large intestine were prepared for microscopic examination, and showed in an unmistakable manner, when examined by the unaided eye, that the affected regions were greatly swollen. On microscopic examination with a low power very extensive ulceration was at once apparent in the diseased areas; these ulcers are always situated on the apices of the rugæ. Overlying the affected regions there are invariably found masses of granular debris containing mucus, blood, disintegrated and disintegrating cells, numerous bacteria, and many amœbæ; small collections of fibrin are occasionally present in this granular material. In the central portions of the areas that are most swollen the ulcerative changes have usually progressed to such an extent that the greater part of the mucosa has entirely sloughed away, and in many instances ulceration completely through this coat, and even down into the submucosa, is found. In the edges of the parts of the mucosa most affected there are numerous

minute areas in which the ulcerative change is just beginning and in which its course and development may be traced with the utmost clearness. The process begins as a catarrhal change in the epithelial cells that line the surface of the intestine; these cells first swell up, become irregular in form, quite granular, their nuclei take the basic stain feebly, and the protoplasm becomes abnormally acidophilic. Following this the cells quickly fall off and disintegrate. The basement membranes upon which they lie next give way, and the tissues between the glands are in this way directly exposed and brought in contact with the contents of the gut. Simultaneously with the shedding off of the epithelial cells the lymph spaces that lie in the tissue beneath become enormously enlarged and filled with fluids, and, the bloodvessels also dilating, the tissues are greatly swollen as a result. It quite commonly happens that some of the distended bloodvessels burst, and in this way red blood cells are found numerous present within the tissues, and as soon as the basement membrane gives way quantities of blood pass out and become mixed with the mucus and other contents of the bowel. Following this, numerous cellular elements collect in the swollen tissues, these consisting, in the early stages, of lymphoid cells and large phagocytes of Metschnikoff (epithelioid cells), mixed with which there are a few connective tissue cells and plasma cells. These alterations extend downward between the crypts; ulceration of the affected tissues rapidly ensues, and in a short time, the glands no longer having support, drop out and become intermingled with the granular debris that lies on the surface of the gut. When this stage is reached the lumina of the crypts are always much diminished in size, owing to the pressure produced by the collections of cells and fluids in the intervening tissues. Even under these conditions the cells that line the crypts show remarkably little change, as the glands are often preserved practically intact when completely surrounded by masses of necrotic material; the cells lining the crypts, however, appear somewhat swollen, their nuclei are larger than normal, and mitotic figures are scarcely ever observed. A more marked alteration than any of these just referred to consists in the fact that the cells have apparently in a large measure ceased to secrete mucin, this substance never appear-

ing as the small, oval masses seen in the normal glands, but when it occurs at all is present rather diffusely within the protoplasm of the cells. In some instances, after the crypts have sloughed completely away from the mucosa and the basement membranes and surrounding tissues have been destroyed, the cells appear in small, irregular collections, but still preserve to a great degree the peculiarities that they exhibit in a normal condition. Lying upon the surface of these newly affected areas, and sometimes in the tissues a short distance from the surface, amœbæ are invariably found; although in a microscopic section only a few of them, as a rule, are present, the number in the affected portion of the mucosa must be considerable. As has just been stated, the amœbæ may be present only upon the surface of the tissues and not lying within them; from this it must be admitted that if they be the real causative agents in this disease they undoubtedly act by means of some toxin produced, and not at all, as one would be inclined to suppose, in a mechanical way.

Where the changes have gone on more extensively the mucosa has in some instances entirely sloughed away, and, more rarely, the ulcerative process has extended even into the submucosa. Under these circumstances there are always found over the surface of the diseased tissues—even in greater amount than over the recent ulcers—masses of granular material containing degenerating cells of all kinds, mucus, many bacteria, and numerous amœbæ. The tissues constituting the surfaces of these ulcers consist almost wholly of cells, the muscular and elastic tissues of the upper part of the submucosa having entirely disappeared, owing to the enormous cellular accumulations in the parts. It is noteworthy, however, that the muscular tissues of the muscularis mucosæ so far preserve their integrity in many instances as to be still distinguishable, while the underlying structures of the submucosa have practically disappeared. These cellular accumulations consist of quite a number of polymorphonuclear leucocytes, many lymphoid cells, a few plasma cells, an occasional mucinoblast, numerous red blood cells, and enormous numbers of the large phagocytes of Metschnikoff (epithelioid cells). In the upper part of this layer amœbæ are frequently found intermixed with the cells just described, and a few bacteria are also some-

times present. Mucinoblasts, as above stated, are found in the diseased tissues, but their number is somewhat less than in the normal parts of the intestine. On either side of these areas, and downward more deeply in the submucosa, the cells gradually diminish in number, and give way to the normal tissues of the part. In those situations where the ulceration extends beneath the muscularis mucosae there are found intermingled with the cells the remains of the original connective tissues of the parts. The elastic tissues have apparently disappeared, for no structures are present that stain either by Weigert's method or by the hæmatoxylin process described in the opening chapter of this essay. There are, however, a number of elongated, irregularly shaped masses in these situations that react feebly to the stains for white fibrous tissue, and which appear to be the degenerate remains of these structures; these masses are much thicker than are the fibres of collagenous tissue found in the submucosa, and around their edges they are almost universally exceedingly ragged and their margins are ill-defined. Quite often the connective tissues have evidently completely disintegrated, as there are found between the cells small granular masses that, from their forms, apparently represent these structures. Deeper down the elastic tissues are still no longer found, but many swollen fibrils of collagenous tissue are always present. As has been before remarked, the cells that are so numerous present at the surfaces of the ulcers and in their immediate vicinity gradually diminish deeper down in the tissues and to either side of the lesions, but even in situations so remote that none of these cells are present the elastic tissue stains very poorly, and the collagenous tissue fibrils are swollen here and there. In the tissues bordering on the ulcers the bloodvessels, especially the veins, are somewhat dilated, but the change is not so marked as one would be led to suppose from the nature of the lesions. The walls of the vessels very near the surfaces are swollen, the elastic tissue fibrils within their coats no longer take their specific stains, and the muscular fibres stain rather diffusely and no longer present the well-defined outlines that characterized them in health. These changes are always most marked on the sides of the vessels nearest the ulcers. A much more pronounced condition is the enormous dilatation of

the lymphatics, and the presence within them of many red blood cells and leucocytes, and, in almost every instance, masses of desquamated epithelial cells that originally lined these channels. These desquamated epithelial cells are enormously enlarged; so much so that they are about the size of the cells lining the crypts. They are very irregular in form and are acidophilic throughout, though with strong basic dyes their nuclei can usually be distinguished. In some instances these cells are so numerously present that they completely block up the lymph channels. The submucosa is always swollen to quite a distance beyond the ulcers, and the greatly dilated lymph spaces in these regions generally contain numerous red blood cells. In no case have the changes extended beneath the submucosa, but in most instances the lymph spaces are dilated and contain numerous blood cells and a few lymphoid cells even down to the circular muscular layer.

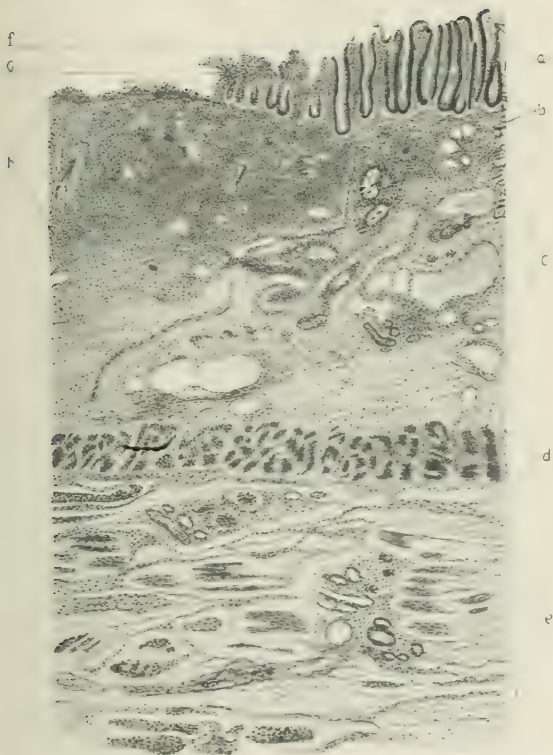
**EXPERIMENTS II. AND III. Duration, fourteen and sixteen days, respectively.**

The two other puppies that had received injections of dysenteric material simultaneously with the one referred to in Experiment I. showed similar evidences of having contracted dysentery. Both developed diarrhoea two or three days after the injections were given, and a few days later the stools contained quantities of mucus and blood in which there were numerous living amœbæ. However, the animal that died in fourteen days did not exhibit such severe symptoms as the other, and, although considerably emaciated, had not lost so much flesh. The earlier death of this puppy is in keeping with the clinical history of the disease as it is observed in man, as it frequently happens that those apparently but little affected die before those who seem to have the malady in a much severer form. As soon as the puppy just referred to was found dead an autopsy was made, with the following results:

The large intestine was empty and its mucosa hyperæmic throughout. The mucous coat was apparently ulcerated away several inches above the anus, and many small ulcers were observed in the upper part of the gut, even up to the margin of the ileocecal valve. The edges of these ulcers were raised slightly above the



# PLATE III.



Specimen from the lower portion of the large intestine of a puppy, into the rectum of which a small amount of fecal material containing living amebæ had been injected four days previously. The tissues were fixed in Bensley's solution and stained with hemalum and eosin. Beck  $\frac{1}{2}$  inch. Oc. 1 inch. *a*. Mucosa, which is entirely absent on the left side of the drawing. *b*. Muscularis mucosæ, the tissues of which show great alteration beneath the point where the mucosa is absent. *c*. Submucosa, which is swollen and contains beneath the ulcerated area multitudes of large phagocytes, many polymorphonuclear leucocytes, a few lymphoid cells, plasma cells, mucinoblasts, and amebæ (*h*). *d*. Circular muscular layer. *e*. Longitudinal muscular layer. *f*. Beginning necrosis of the surface epithelium at edge of ulcer. *g*. Cellular collection replacing mucosa at the margin of the floor of the lesion. (Exp. I.)





taken from the lower portion of the large intestine of a puppy, into the middle of which a small amount of dysenteric material containing living amebae was injected fourteen days before the death of the animal. The tissues were fixed in Bouley's solution and stained by Benda's iron-hæmatoxylin method. Beck 1000, fig. 1, plate 1, p. 10. Scale, 1 inch. *a*. Mucosa, which is absent at either side of the drawing. *b*. Muscularis, containing many lymphoid cells, numerous plasma cells, and quite a few mucinoblasts; there is much newly-formed fibrous tissue in this layer. *c*. Circular muscular layer. *d*. Longitudinal muscular layer. *e*. Granular debris in the lumen of the intestine. *f*. Layer of newly-formed epithelium. (Exp. II.)



surrounding mucous surface, and in some situations appeared to be slightly undermined; their floors were of a grayish color.

A small abscess about 1 cm. in diameter was found in the substance of the liver just above the gall-bladder; the contents of this abscess were of a grayish color and contained numerous fragmented liver cells, quite a number of polymorphonuclear leucocytes, and a few amoebæ.

Sixteen days after the injection was given the remaining puppy was found in a dying condition. The animal was killed with chloroform and an autopsy was at once made. The puppy was greatly emaciated. On examination the large intestine was found to be empty. The wall of the gut was considerably thickened, and its mucous surface was of a pale pinkish-gray color. The entire mucosa was beset with great numbers of small ulcers—generally 2 mm. or 3 mm. in diameter—that in every way resembled those already described as occurring in the intestines of the other puppies. The ulcers were not more frequently present on the tops of the rugæ than elsewhere on the mucous surface, though it should be remarked that these elevations are not so numerous or well-marked as is usually the case.

The liver contained six small abscesses, the largest being about 0.5 cm. in diameter. These abscesses presented the appearance of those found in the liver of the other puppy.

As the microscopic lesions in the intestines of these two puppies are in every way similar, the description that follows applies to both:

On examination with low powers the mucosa is found to present extensive alterations; indeed, this coat of the intestine is in a large measure absent, there being only here and there small islets in which the normal tissues are more or less preserved. In situations where the changes are least marked mucin formation is going on in the lining cells of the crypts to an unusual extent—none of the cells under these circumstances being free from this substance—and, as is so often the case where the epithelial cells are subjected to irritating influences, the mucin does not occur in the small globular masses as in health, but scattered diffusely throughout the protoplasm of the cells.

In the interstitial tissues lying between the crypts the blood-

vessels are considerably dilated and are filled with blood, and the surrounding lymph spaces are distended, contain many blood cells and an unusual number of lymphoid and plasma cells; the effect of this, of course, is to cause this coat to be considerably swollen. Beneath these areas the muscularis mucosæ generally shows no apparent alteration, but the tissues of the submucosa are always swollen and contain a great many lymphoid cells, and many more than the usual number of mucinoblasts, a quantity of plasma cells, and a very few polymorphonuclear leucocytes. The epithelial cells lining the bloodvessels and lymph spaces are also considerably swollen, as a rule, and not infrequently have shed off from their basement membranes.

At the edges of the areas least affected there are found two distinct classes of lesions, though they at many points merge insensibly into each other. One of these represents recent changes in the mucosa and the other the lesions of a more chronic kind. The former will be first considered.

No extended description of the more recent lesions is necessary, for in those instances where the necrotic process has just begun, or has not been in existence for a great length of time, changes are found that in every way resemble those encountered in the beginning ulcers described in connection with Experiment I.

In the more chronic ulcers the necrotic process has passed through the mucosa in all instances, and extends to a varying distance into the submucosa; in some cases the entire submucosa has sloughed away, but under no circumstances have even the superficial portions of the circular muscular layer undergone ulcerative change. The tissues forming the floors of these lesions, as a rule, are made up of necrotic connective tissue, but in some instances a remarkable development of epithelium has occurred over the exposed surfaces of the ulcers, and in some cases has completely covered them. This layer of epithelium is attached to the tissues that lie beneath, and follows closely the irregularities of its surface; in many instances the cells have grown downward into the tissues, lining what were apparently enlarged lymph spaces, and forming glandular structures that greatly resemble the normal crypts. These newly-formed crypt-like bodies have their bases sometimes on the circular muscular

coat, and not infrequently extend out laterally for quite a distance into the submucosa. The cells constituting this newly-formed epithelial covering of the ulcers, and those found in the newly-formed crypt-like bodies, resemble very greatly the normal epithelial cells on the free surfaces of the intestine. They occur in a single layer, and consist of tall, well-defined, columnar epithelial cells, the nuclei and protoplasm of which stain in the usual way, but under no circumstances does mucin formation appear to go on within them. Mitotic figures are never observed in these cells.

The tissues lying beneath these ulcers consist of numerous very dense bodies of white fibrous tissue and quite a number of fibrils of elastic tissue. The white fibrous tissue has evidently increased in amount, as it is present in considerably greater quantity than is found in the normal submucosa. The lymph spaces in these situations contain very little fluid and never appear unusually dilated. Scattered throughout the tissues there are great numbers of lymphoid cells, many plasma cells, and a very unusual number of mucinoblasts; there are also a few more or less degenerate connective tissue cells and an occasional polymorphonuclear leucocyte. The bloodvessels are not particularly numerous and never appear dilated in these areas; it may be noted, however, that the epithelial cells lining the bloodvessels and the larger lymph channel generally appear swollen, and, especially in the latter, have oftentimes shed off from their basement membranes. Fibrin is never found in these tissues, nor have bacteria been demonstrated in any of the specimens examined.

The circular muscular layer shows no alteration further than that there is an unusual number of mucinoblasts lying between the muscle fibres.

The longitudinal muscular layer and subserous and serous coats appear entirely normal.

From the foregoing description of the changes that occur in experimental dysentery in dogs it will be seen that the lymph nodes of the intestinal wall show no peculiar or striking alterations in this disease, and, indeed, it may be said that these structures are always, as it were, incidentally affected, and that they never show alterations of a more pronounced kind than are seen in the neighboring tissues.

It will be recalled that abscesses were present in the livers of both of the puppies.

On microscopic examination it was found that the contents of these abscesses consisted of degenerate liver cells, considerable numbers of polymorphonuclear leucocytes, and, in some situations, degenerated red blood cells. The necrotic liver cells frequently formed long, irregular rods, rounded at the ends, that greatly resembled those masses that result from the breaking up of hepatic cells in the liver of man under similar conditions. In properly stained sections a few bacilli may be demonstrated, and a small number of amœbæ are here and there found. These abscesses were evidently recent, for their walls consist merely of compressed liver cells that are more or less necrotic. The hepatic cells in the vicinity of the abscesses show evidences of beginning degeneration, but there is not that wide-spread and very marked necrosis of these cells that occurs in amœbic abscesses of the liver in man. The capillaries in the vicinity of the abscesses are filled with polymorphonuclear leucocytes, and, in many instances, apparently contain no red blood cells at all; further away the capillaries are distended with blood and are somewhat dilated, but these alterations are by no means marked.

#### EXPERIMENT IV. **Duration, sixteen days.**

A puppy, twenty-six days old, was injected with fecal material containing living amœbæ. In a few days the animal developed dysentery and died in sixteen days after the dysenteric material had been administered. Its intestine presented changes in every way similar to those found in Experiments II. and III.

#### **Résumé of the Alterations found in the Large Intestines of Dogs Suffering with Experimental Dysentery.**

On post-mortem examination the large intestines were in all cases found swollen and the mucosa somewhat reddened in the affected regions. There were scattered over the surface numerous small ulcers, these being limited to the lower part of the small intestine in the case where the animal was killed; but in those instances where death resulted from the disease these lesions were



observed on all parts of the surface of the bowel. In two of the cases there were liver abscesses.

On microscopic examination considerable alterations are apparent in the intestinal walls. Where the lesions are only beginning there are merely slight catarrhal changes in the surface epithelium, in the immediate vicinity of which amœbæ are invariably found. At a later stage the epithelial cells entirely desquamate and their basement membranes disappear. Simultaneously the interglandular tissues beneath become greatly swollen as a result of the accumulation of liquids in the parts and of the dilatation of the bloodvessels; in many instances the walls of the vessels burst, and hemorrhage occurs in the parts. In addition to the pre-existing cells normally found in these situations great numbers of large phagocytes of Metschnikoff quickly collect. Following this, ulceration begins from above, and, extending downward between the glands, continues until these structures, no longer having support, drop out of the intestinal wall.

The muscularis mucosæ resists the process decidedly, but in many instances the tissues composing it have likewise become necrotic and have sloughed away; under these circumstances the ulcers extend into the tissues of the submucosa. It is, however, often the case that remnants of the muscularis mucosæ are found in situations where both the tissues above and below are entirely necrotic. The floors of these deeper ulcers consist of the remains of the pre-existing tissues of the parts, intermingled with which there are multitudes of the large phagocytes of Metschnikoff, many polymorphonuclear leucocytes, and a few lymphoid cells, plasma cells, and mucinoblasts. It is particularly noteworthy that while all of the connective tissues in these situations undergo rapid alteration, the elastin suffers more than the collagenous tissues and very quickly disappears.

In the more chronic lesions similar alterations are found, with the exception only that the large phagocytes have given way to great numbers of plasma cells, and that fibrous tissue is being formed in considerable quantities.

In no instance has the necrotic process extended into the circular muscular layer.



## PART IV.

EXPERIMENTAL PRODUCTION OF CHANGES IN  
THE LARGE INTESTINES OF DOGS BY MEANS  
OF HEAT AND BY THE INJECTION INTO  
THEM OF VARIOUS IRRIGATING  
SUBSTANCES.



## PART IV.

### EXPERIMENTAL PRODUCTION OF CHANGES IN THE LARGE INTESTINES OF DOGS BY MEANS OF HEAT AND BY THE INJECTION INTO THEM OF VARIOUS IRRITATING SUBSTANCES.

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BY no means all of the experiments that have been made upon the large intestines of dogs with irritants are recorded in the following pages, for more than one test has been made in almost every instance, and in some cases four, six, eight, and even ten animals were sacrificed before a definite conclusion was arrived at as to the character of the lesions induced by the irritants in question. It was very early patent that should an attempt be made to describe the changes found in every animal experimented upon that this essay would be extended to an entirely unnecessary length, and it has therefore been the aim of the writer to select for record out of the several experiments made with each substance the one that appeared most typical.

## CHAPTER I.

### EXPERIMENTS TO DETERMINE THE EFFECTS OF A HIGH DEGREE OF HEAT ON THE LARGE INTESTINES OF DOGS.

#### EXPERIMENT I. **Intestine burned after death.**

A KNIFE was heated to a dull cherry-red color, and the sharp edge was lightly pressed for a moment against the mucosa of the large intestine of a dog after its removal from the animal's body. Where the knife came in contact with the tissue a scarcely perceptible grayish line was produced on its surface.

Microscopic specimens were prepared in the usual way, and on examination the following changes were noted: At the points where the burns were made there are distinct depressions upon the surface of the mucosa. Covering these depressed areas there are layers of finely granular material containing small particles of mucin; this substance, however, lies all along the free surface of the intestine, and is here evidently not the result of the action of heat. After being stained by the usual methods the mucosa is found to be divided into four more or less distinct layers in the areas beneath the points where the burns were made. The first of these (*a*) lies immediately beneath the granular material just described, and consists of the tissues that have suffered most from the effects of the heat. Beneath this (*b*) there is an area that is almost entirely empty. Still further down (*c*) the tissues exhibit marked changes and present certain staining peculiarities hereafter to be referred to. The bases of the glands have not suffered so greatly as the tissues higher up, and, as a consequence, present almost a normal appearance and form the lowest layer (*d*) of the mucosa. The finer changes occurring in these different layers will now be considered in the order in which they have been mentioned.

(a) The tissues near the free surface of the mucosa exhibit marked alterations. The outer portion of this layer, which is in immediate contact with the granular material just referred to, consists of tissues that have in a large measure lost their nuclei and that stain in an almost uniform manner with acid dyes. The connective tissue fibrils are here fused together, forming highly granular, acidophilic masses in which the original cellular structures cannot be recognized. At a very short distance from the surface the tissues contain cells the nuclei of which stain even more intensely than normal with basic dyes. These nuclei, which evidently belong to the cells lying in the connective tissue, are considerably elongated and their long axes usually lie parallel to the surface of the intestine. The connective tissue fibrils preserve here their usual appearance in a degree, but are swollen and usually greatly distorted. In the lower portion of this badly burned area there are always one or two of the crypts of Lieberkuehn, the ends of which have evidently been turned over by the pressure exerted by the knife while the burn was being made. The crypts contain hardly a vestige of the epithelial cells that originally lined them. At the edges of the burnt area the epithelial cells in the crypts have not undergone such extensive alterations, but it is noteworthy that the mucin is far better preserved than any of the other constituents of the cells. The nuclei of the cells lying between the crypts in the deepest portion of the badly burned region show a certain degree of elongation, but their long axes are usually transverse to the surface of the gut. The connective tissues are here likewise considerably swollen.

(b) The open spaces beneath the areas just described lie on a level that about corresponds to the necks of the crypts; in the fresh state they probably contained a certain amount of steam, and, if not this, certainly more or less liquids, as they are in a great measure empty. In no instance, however, do they entirely separate the deeper tissues from those that lie above, for at some points small strands of collagenous tissue pass through the cavities and unite them together. The tissues that line the spaces present an exceedingly ragged appearance on all sides, indicating in an unmistakable manner that they were violently torn asunder.



(c) The tissues that lie beneath these cavities are not so much altered as those nearer the surface, but nevertheless present a considerable degree of change. The crypts, where they abut on the open spaces, are always diminished in calibre owing to swelling of the structures that lie between them. In these situations the external coats of the epithelial cells lining the crypts have universally ruptured, and the cells have the appearance of being fused together; their nuclei are irregular in form, being elongated and often twisted, and take the basic stain feebly. It is a curious fact that the masses of mucin that normally occur in the cells in these situations preserve their form, and, in most instances, even their relative position to each other. The lumina of many of the crypts are completely filled with free mucin and disintegrated cells. Lower down the cells of the crypts still present no distinct outlines. The nuclei of these cells are very much elongated and their long axes are always parallel, or nearly so, to the long axes of the crypts; they take the basic stain with great intensity. The connective tissues that intervene between the crypts at some distance from the open spaces do not show a great degree of change, but both the collagenous and elastic tissue fibres take the stain poorly, and they are in many instances swollen. The lymph spaces between the fibres are distinctly increased in size and evidently contained either small quantities of water or, what seemed much more likely, minute collections of steam; the cells that lie in these situations are irregular in form and are oftentimes decidedly swollen. The cells found in the interstitial tissues at these points, however, as a rule, show no alteration, and it is to be especially noted that their nuclei do not show that elongation that invariably occurs in the neighboring epithelial cells.

(d) The epithelial cells lining the bodies of the crypts in the areas just beneath where the burns were made have generally desquamated, and in many instances the walls of the cells have ruptured, the lumina of the crypts contain quantities of granular debris that results from this process. In these instances, however, in which the cells contain mucin this substance presents an entirely normal appearance. The tissues intervening between the bases of the crypts show no alteration.

The other coats of the intestine are entirely unaltered.

Quite a number of specimens were prepared and examined that were burned with the sharp edge of a knife fifteen minutes before the death of the animal whose intestine was being operated upon.

On microscopic examination none of these showed alterations different in any way from those found in instances where the intestine was burned after death, and a separate description of the changes is therefore considered unnecessary.

Other specimens were prepared by burning the intestine in a similar manner six hours before death. On microscopic examination the alterations are found to agree in every particular with those already described, with the exception only that the bloodvessels in the vicinity are dilated and in many cases ruptured, and that the tissues at the edges of and immediately beneath the lesions are found to be somewhat swollen as the result of the presence of a certain amount of effused blood, from the collection in the parts of fluids, and the presence of quite a number of polymorphonuclear leucocytes; these changes are confined to the immediate vicinity of the alterations and do not extend to any great distance into the surrounding tissues.

#### EXPERIMENT II. **Heat. Duration, six hours.**

The blade of a knife was heated to a cherry-red color, and its flat surface was applied for a moment to the mucous surface of a dog's intestine. Six hours later the tissue was removed. The wall of the gut at the point where the burn was made was distinctly swollen; the surface of the intestine was of a grayish color, and surrounded by an area of marked redness.

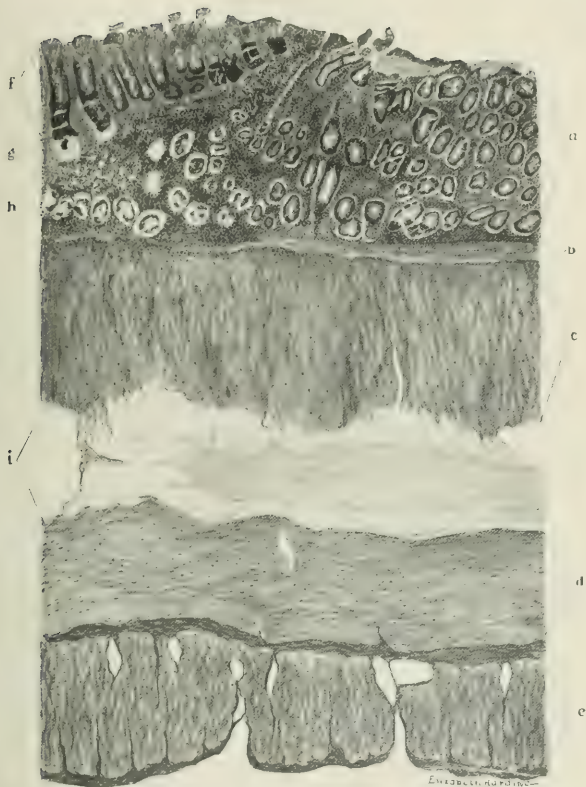
On microscopic examination it is found that the tissues lying at a short distance from the edge of the burn show no alteration.

Somewhat nearer the only changes found are a dilatation of the bloodvessels of the interglandular substance, and as the margin of the burnt area is approached it is found that, in addition to the dilatation of the bloodvessels, quite a number of polymorphonuclear leucocytes have collected in the parts, and the epithelial cells covering the surface of the mucosa and those lining the underlying crypts exhibit catarrhal change; the capsules of these desquamated cells seem to have ruptured in many instances, and the pro-

toplasm has been discharged, leaving the nucleus in an apparently normal condition. The deeper tissues of the intestinal wall show beneath these areas practically no change. In the edges of the burnt region the pre-existing tissues have completely disappeared; the epithelial cells that covered the surface, and those that lined the crypts, and the interglandular substance have all entirely disintegrated, and in their stead there is found a mass of polymorphonuclear leucocytes, lymphoid cells, pseudoplasma cells, and a few mucinoblasts. It is rather remarkable that in this zone not even a vestige of the crypts remains. Similar alterations are present in the muscularis mucosæ, the fibrils of which have been almost entirely replaced by cellular collections corresponding to those found more superficially. The tissues of the submucosa lying immediately beneath are considerably swollen, this being the result of the accumulation of fluids in the parts and of the presence of a considerable amount of hemorrhage; there are likewise found here a few polymorphonuclear leucocytes, quite a number of lymphoid cells, many plasma cells, and a few large phagocytes and mucinoblasts. The red blood-corpuscles that have been effused into the tissues have generally, in greater or less degree, degenerated, so that there is often found an acidophilic granular débris representing them. The tissues contain also a great amount of fibrin. The pre-existing collagenous tissues of the parts stain in an almost normal manner and the elastic tissue fibrils exhibit no alteration.

The layer of the submucosa above described in which the pre-existing tissues have been entirely replaced by cells is exceedingly thin, measuring, as a rule, not more than  $100\mu$  in thickness. Internal to it—*i. e.*, toward the central portion of the burn—the superficial structures, with the exception of the surface epithelium, still remain in their normal situations, and, though greatly altered, may be always recognized; the surface epithelial layer, and the basement membrane upon which the cells lie, have entirely disappeared. The tissues lying on and near the surface have been so altered that they have lost, in a large measure, the property of taking basic stains, and appear as an almost homogeneous, hyaline layer occupying the outer half of the mucosa. In the lower portion of this layer particles of mucin lying within

PLATE V.



Specimen from about the middle portion of the large intestine of a dog that had been burnt six hours before removal from the animal's body with the flat side of a knife heated to a cherry-red color. The tissue was fixed in Bensley's solution and stained by the method of Van Gieson. Beck  $\frac{3}{4}$  inch, Oc. 1 inch. *a*. Mucosa. *b*. Muscularis mucosæ. *c*. Submucosa. *d*. Circular muscular layer. *e*. Longitudinal muscular layer. *f*. Edge of the burnt area in mucosa. *g*. Masses of cells separating the burnt tissues from those that are but little changed. *h*. Masses of desquamated epithelium in the deeper portions of the crypts below the burnt area. *i*. A collection of albuminous liquid containing fibrin separating the submucosa from the circular muscular layer. (Exp. II.)



the remnants of the epithelial cells still stain in a normal way. This hyaline coat gradually merges into a layer in which the cells have been evidently fixed by heat after a fashion ; the tissues here preserve in a large measure their normal appearance and take basic stains in the usual way. On close inspection it is invariably found that the epithelial cells lining the crypts have apparently amalgamated together, and that their nuclei are often greatly distorted ; in many instances these nuclei are rod-shaped and their long axes lie parallel to the long axes of the crypts in which they lie. The mucin in the mucin-bearing cells stains in a normal way. The glands are much compressed as a result of the alterations in the intervening substance at these points.

The bloodvessels of the interglandular substance lying between the partially preserved glands just described have universally ruptured, and there is often present great quantities of disintegrated blood in these tissues. In addition to the cells that are normally found in the parts there are also numerous polymorphonuclear leucocytes. The elastic tissues found in this region are excellently preserved, but the collagenous tissues have entirely disappeared.

The basal portions of the glands show alterations similar to those that were described as occurring throughout the glands immediately surrounding the burnt area. These changes consist in shedding off of the epithelial cells and the disappearance of their protoplasm, leaving in most instances the nuclei intact. The basement membranes upon which these cells lie are normal.

The interglandular substance surrounding the deeper portions of the crypts is composed of the cells that are normally found in the parts, with the addition of a considerable amount of hemorrhage and many polymorphonuclear leucocytes.

The fibres of the muscularis mucosae have been in a large measure replaced by polymorphonuclear leucocytes, the tissues composing this layer apparently having undergone solution and disappeared.

The tissues of the submucosa that lie immediately beneath the muscularis mucosae are greatly swollen ; this is a result of the presence of fluids and of great numbers of polymorphonuclear leucocytes. The bloodvessels in these situations are dilated and

filled with blood, and multitudes of polymorphonuclear leucocytes are always attached to the inner coats and in many instances may be seen lying within their walls. There is a small amount of hemorrhage in these tissues. Both the collagenous and elastic tissue fibrils stain well. The tissues constituting the deeper portions of the submucosa are likewise greatly swollen, this being the result in a large measure of extensive hemorrhages into the parts. The red blood-corpuscles are usually in a partially degenerate condition wherever they are found lying loosely in the tissues of the submucosa. In the deeper portions of the submucosa there are extensive deposits of fibrin.

The circular muscular layer and the submucosa have been torn asunder by the accumulation between them of great quantities of an albuminous liquid; this liquid contains fibrin, but practically no cells.

The remaining coats of the intestine show no alteration.

### **Résumé of the Changes Produced in the Dead Tissues by Heat.**

As a result of the changes described the burnt tissues present quite a characteristic general appearance under low powers of the microscope; externally they contain practically no nuclei, and all of the structures present stain with acid dyes. Somewhat lower down numerous cells are present, the nuclei of which stain with great intensity with basic dyes, and the intervening tissues are normally acidophilic. Beneath this there is an open space through which run shreds of more or less altered connective tissue. Still lower down there is an area in which the nuclei of the epithelial cells are much elongated, have their long axes parallel to the long axes of the glands, and stain very poorly, and the lumina of the crypts are filled with the granular debris that results from the disintegration of the epithelial cells. The intervening connective tissue is swollen, oftentimes to such an extent that the upper portions of the lumina of the crypts are almost entirely obliterated. Somewhat beneath this, and forming the lower border of this layer, the nuclei are stained with considerable intensity, but in every other way the cells of the crypts resemble those of the portions of the glands higher up. The



cells that lie in the bases of the crypts have in many instances degenerated and have very generally shed off from their basement membranes.

### Changes Produced in the Living Tissues by Heat.

Where the knife came in actual contact with the tissues they were completely destroyed and have entirely disappeared. The structures beneath were acted upon in such a way that they have become practically acidophilic throughout; they have in a large measure lost their morphologic peculiarities, and appear as a more or less homogeneous, hyaline mass covering over the partially preserved tissues that lie underneath. As might be expected, the collagenous tissue fibrils can no longer be recognized, but the threads of elastic tissue stain in a more or less normal way. The only portions of the epithelial cells that are preserved in the parts are the particles of mucin contained within some of them. Lower down these almost completely destroyed tissues merge into structures that are fairly well preserved, the heat having acted to a certain extent upon them as a fixative. In this area the epithelial cells lining the crypts appear to have coalesced, and their nuclei are greatly distorted. Sometimes these nuclei are rod-shaped, and they not uncommonly lie with their long axes parallel to the long axes of the crypts. The basement membranes of these portions of the glands are normal.

The tissues that normally intervened between these glands have been in a large measure replaced by blood, which has been effused into the parts in great quantities; the pre-existing cells of the part are present in about the usual number.

Lower down in the glands the epithelial cells have shed off, the cellular membranes appear to have ruptured in most instances, and the protoplasm, as a consequence, has been liberated.

In the intervening tissues there are large numbers of polymorphonuclear leucocytes.

Beneath the burnt areas the fibres composing the muscularis mucosæ have in a large measure disappeared, but the elastic tissue fibrils appear to have suffered no change. Replacing the muscle fibres there are a great many polymorphonuclear leucocytes.

The portions of the submucosa that lie in the vicinity of the muscularis mucosae are swollen, contain great numbers of polymorphonuclear leucocytes, and quite an amount of free blood. The deeper layers of this coat contain enormous quantities of disintegrating blood and much fibrin. Albuminous fluids have collected in considerable quantity between the submucosa and the circular muscular layer.

None of the other coats of the intestine presents abnormalities.

Immediately around the edges of the burnt area the pre-existing tissues of the mucosa have entirely disappeared, being replaced by polymorphonuclear leucocytes in a large degree. Somewhat further outward the bloodvessels are dilated, and there is quite an amount of hemorrhage into the tissues.

## CHAPTER II.

### EXPERIMENTS TO DETERMINE THE EFFECTS PRODUCED ON THE LARGE INTESTINES OF DOGS BY THE INJECTION OF ALKALINE SOLUTIONS.

#### EXPERIMENT I. *Dilute liquor potassæ.* Duration, twelve hours.

ON January 31, 1900, there were injected into the rectum of a dog 10 c.c. of liquor potassæ (U. S. P.), diluted with an equal quantity of water. Twelve hours later the animal was killed with chloroform, and an autopsy was at once made.

On examination the lower part of the intestine was found to be almost empty, and the mucosa was uniformly reddened. In this situation there were many transverse rugæ on the surface of the gut, the apices of which showed no more redness than the surrounding surface of the intestine.

On microscopic examination it is found that the superficial epithelium that normally covered the mucosa has entirely disappeared in the affected region, and the outer half of this coat is in a semi-necrotic condition. The epithelial cells lying in this situation have entirely disintegrated, and there remains in their stead a mass of granular débris, intermingled with which there is much mucin in all instances; however, the mucin here found does not stain altogether so brilliantly as that present in the lower part of the crypts, and it is evident that it is more or less altered. The average diameter of the crypts in this situation is decidedly decreased, this being due to the accumulation of cells and fluids in the interglandular substance. In this part of the mucosa the elastic basement membranes have in all instances entirely disappeared. The tissues that lie between the crypts are in a large measure acidophilic, the only exception to this being the nuclei of the polymorphonuclear leucocytes that evidently migrated into the parts after the maximum deleterious action of

the liquor potassæ had passed away. The bands of pre-existing collagenous tissue can always be made out in the diseased situations; they are distinctly swollen and do not present the sharp outlines that they exhibit in health. The pre-existing lymphoid cells, the pseudoplasma cells, and the mucinoblasts that are normally found in these situations have become entirely necrotic, and, as before remarked, the only cellular constituents that appear normal are the multitudes of polymorphonuclear leucocytes that have penetrated into the parts. The walls of the bloodvessels have likewise undergone a complete necrotic change, and much of the blood that was contained in them has been widely diffused into the interstices of the interglandular substance; in many situations masses of partially degenerated red blood-cells may be found lying loosely in the tissues, but these cells have, as a rule, become so completely necrotic that they can no longer be recognized with certainty.

The epithelial cells that line the crypts in the area immediately beneath the necrotic layer just described present the usual changes that occur when they are subjected to irritation, being swollen, irregular in form, and in many instances completely detached from their basement membranes, and lie loosely in the lumina of the crypts. Some of them have evidently entirely disintegrated, for there is always present a considerable quantity of granular débris surrounding them. Within the lumina of the crypts there is invariably found much mucin. In some instances mucin formation has gone on to such a degree that this substance completely fills the lumina of the crypts, and has exerted such a pressure upon the surrounding cells that they appear greatly diminished in size and lie compressed against their more or less necrotic basement membranes; under these circumstances those nuclei of the cells that are oblong lie parallel to the long axes of the crypt, and not transversely as in health. In instances where the mucin formation has been extreme almost the entire crypt is taken up by the plugs of mucin that lie within them, these measuring in diameter oftentimes as much as  $60\mu$ —but a few microns less than the entire gland. None of the epithelial cells that are found in this area ever show in their protoplasm any evidence of mucin being present. The cells lining the basal portions of the crypts

generally appear somewhat swollen, and in some instances they have shed off from their basement membranes ; but further than this no alteration in these parts of the glands is apparent. The basement membranes that line the bases of the crypts still stain in a fairly normal way, but the tissues of which they are composed lose their power of taking the usual dyes a short distance from the deepest portion of the glands. In the interstitial tissues lying immediately beneath the necrotic area the bloodvessels are enormously enlarged and are filled with blood, but further than this the tissues practically present no alteration. The line of demarcation between the diseased tissues and those that lie beneath them is always exceedingly abrupt. The tissues lying beneath the basal portions of the glands show no alterations.

The muscularis mucosæ is normal.

The bloodvessels lying in the portion of the submucosa in the vicinity of the muscularis mucosæ are generally somewhat dilated and are filled with blood. No other change is found in the submucosa.

The other coats are entirely normal.

## EXPERIMENT II. *Liquor potassæ.* Duration, twenty-four hours.

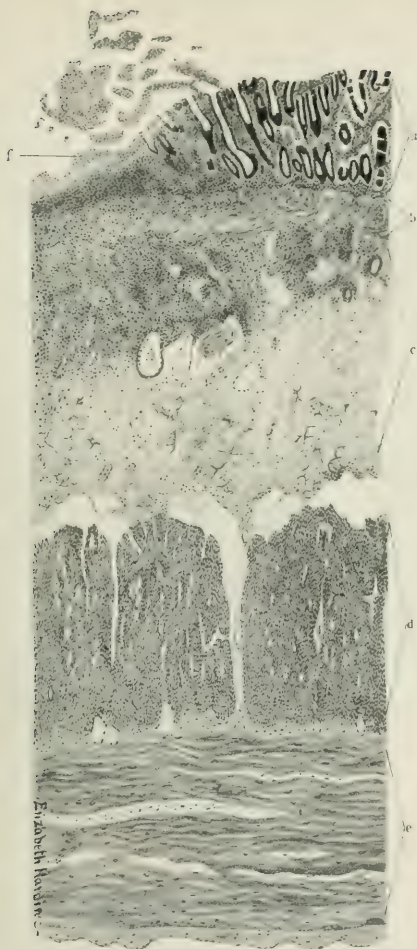
At 1 P. M., on November 27, 1900, 10 c.c. of liquor potassæ were injected into the rectum of a dog weighing about 6 kg. Twenty-four hours later the animal was killed with chloroform, and an autopsy was at once made. The large intestine was empty, but only the lower half showed obvious alteration. In this region the mucosa was covered with a thick layer of mucus, and its surface presented a grayish appearance, mottled with small, pinkish-colored spots. The rugæ were largely obliterated, and even where present the changes were no more marked on their tops than in other parts of the neighboring mucosa.

On microscopic examination the surface layer of epithelium covering the mucosa is found to be generally absent, though small areas are here and there found in which the epithelial cells have not desquamated and appear entirely normal. Where the surface epithelium shows no change the tissues that lie beneath are prac-

tically unaltered, with some exceptions hereafter to be referred to, and for this reason description is only necessary for those regions in which superficial necrosis of the epithelium has occurred. The changes in the mucosa vary much in different situations, there being in some places necrosis only of the surface epithelium and of the lining cells of the mouths of the crypts, while in others the entire mucosa is destroyed. In some areas the mucosa is represented by a mass of cells intermixed with which is much granular debris, the elements normal to the parts having completely sloughed away. Lying along the free surface of the intestine there are always found collections of epithelial cells and polymorphonuclear leucocytes; these cells do not show any marked degree of alteration, as they preserve in a large measure their normal morphologic peculiarities and stain in the usual way. In those parts of the mucosa where only the upper portions of the crypts have been entirely destroyed the epithelial cells remain attached to their basement membranes and preserve their normal form; it is noteworthy, however, that no mucin is present in these cells, and that their protoplasm stains somewhat more deeply with basic dyes than is normally the case. Mitotic figures are comparatively rare in these cells. In regions where the crypts have been almost entirely destroyed the epithelial cells that appear in the remnants of these structures have shed off from their basement membranes, and are round or irregular in form; they however still preserve their normal staining reactions.

The elastic tissue basement membranes of the diseased crypts no longer take their specific stains, though they can in some instances still be made out as very delicate, finely hyaline structures lying in the situations that they normally occupy.

The changes in the interstitial tissues vary considerably, and depend upon the extent of the alterative process. In those areas where only the superficial epithelium has been eroded away the tissues that lie beneath show practically no alteration with the exception that the bloodvessels are considerably dilated and that there are a few polymorphonuclear leucocytes in the lymph spaces. Where the changes have been more extensive the bloodvessels are in all instances enormously dilated and have not infrequently



Specimen from about the middle portion of the large intestine of a dog into which a dilute solution of liquor potassæ had been injected twenty four hours before the tissues were removed from the animal's body. The tissues were fixed in Bensley's solution and stained with carbol toluidin-blue and eosin. Beck  $\frac{1}{4}$  inch, Oc. 1 inch. *a.* Mucosa, the structures of which have been entirely replaced by polymorphonuclear leucocytes, red blood cells, lymphoid cells, large phagocytes and mucinoblasts at (*f*). *b.* Muscularis mucosæ, which is swollen and contains numerous polymorphonuclear leucocytes. *c.* Submucosa, which is much swollen and contains many polymorphonuclear leucocytes and much fibrin; this layer is partially separated from the circular muscular layer by collections of liquid. *d.* Circular muscular layer. *e.* Longitudinal muscular layer. (Exp. II.)





ruptured. There are found in the tissues, as a consequence, numerous red cells, and there are always present considerable numbers of polymorphonuclear leucocytes; lymphoid cells, large phagocytes (epithelioid cells), and a few plasma cells are likewise encountered. Mucinoblasts are especially large and frequent in all parts of the diseased mucosa. As has been before remarked, these changes frequently extend through the mucous coat, and under these circumstances the surfaces of the resulting ulcers consist of more or less necrotic connective tissue, intermingled with which there are large numbers of cells, principally polymorphonuclear leucocytes.

The muscularis mucosæ is considerably swollen, this being particularly the case in those areas where the necrotic process has extended deeply into the mucosa. The lymph spaces between the muscle fibres are more or less dilated, contain quite a number of polymorphonuclear leucocytes, and in the fresh state were evidently distended with fluids. The muscle fibres of this layer present no obvious alterations, but almost everywhere the elastic tissue fails to take its specific stains.

The submucosa shows a very marked degree of swelling. The lymph spaces are enormously dilated, contain a few polymorphonuclear leucocytes, and large quantities of fibrin. The collagenous tissue in this layer stains in a normal manner, but the fibrils of elastic tissue do not take their specific stains. These changes are universally present in all parts of the submucosa examined—even beneath those areas where the tissues lying above are entirely normal.

The muscular, subserous, and serous coats show no change.

### EXPERIMENT III. *Liquor potassæ.* Duration, twenty days.

On December 11, 1900, a dog weighing about 5 kg. was given 10 c.c. of liquor potassæ (U. S. P.) by the rectum. On the following day the animal appeared perfectly well, and had apparently suffered no ill effect as a result of the administration of the drug. On December 14th the injection was repeated. On the following day the dog passed a considerable quantity of bloody mucus and presented unmistakable evidence of being ill. On December 17th

10 c.c. of liquor potassæ were again administered. No more injections were given until December 23d, for the reason that the dog that was receiving the acid injections was so weak that it appeared unwise to repeat the dose earlier, and it was thought best for the sake of uniformity to make the administrations of the acid and alkali correspond as closely as possible. Another injection was given on December 28th. On December 31st the animal was killed with chloroform, and an autopsy was at once made. The lower half of the large intestine was found empty, but the upper portion contained a small amount of fecal matter. The walls of the lower half of the gut appeared somewhat thickened. The transverse rugæ in this situation were quite prominent, but the mucous membrane covering their apices did not appear so red as that found on the intervening portions of the surface of the intestine; although the entire mucosa appeared decidedly discolored, there was at no point appearance of ulceration.

On microscopic examination it is found that the surface of the gut is beset with numerous ulcers—the mucosa in these areas being always practically destroyed—while the intervening portions show, as a rule, but little change; indeed, it may be said that the entire wall of the gut is normal in those areas where ulceration does not exist—if a mild degree of dilatation of the vessels that lie between the crypts be excepted. At the margins of the ulcers this practically normal mucosa ceases abruptly, and it is noteworthy that the epithelial cells lining the crypts, as well as the intervening surfaces, show even at the very edges of the lesions no alterations of moment. In the ulcerated regions the mucosa has in almost every instance entirely disappeared, though here and there the basal portions of the glands are, although much altered, still preserved. The epithelial cells that lined these remnants of Lieberkuehn's crypts have, under these circumstances, largely desquamated, and in all stages of disintegration lie grouped together in the lumina of the glands. Mixed with these necrotic cells a small amount of free mucin is sometimes found. Occasionally a new formation of epithelial cells has occurred in these vestiges of the crypts; under such circumstances the newly-formed cells are flattened, are exceedingly irregular in form, and within them no mucin is found.

# PLATE VII.



Specimen from about the middle portion of the large intestine of a dog into which a dilute solution of liquor potassæ had been injected twenty days before the tissues were removed from the animal's body. The tissues were fixed in Bensley's solution, and stained with carbol toluidin-blue and eosin. Beck  $\frac{1}{4}$  inch, Oc. 1 inch. *a*. Mucosa, the structures of which have been replaced by polymorphonuclear leucocytes at (*f*). *b*. Muscularis mucosæ, which is swollen and contains quite a number of polymorphonuclear leucocytes in some situations. *c*. Submucosa, which is swollen, contains numerous polymorphonuclear leucocytes, mucinoblasts, lymphoid cells, and many plasma cells. *d*. Circular muscular layer. *e*. Longitudinal muscular layer. (Exp. III.)



The tissues that originally lay between the crypts have practically disappeared, but there remains in their stead an enormous number of polymorphonuclear leucocytes, mixed with which there are a few lymphoid cells. These cellular masses forming the coverings of the ulcers are always considerably thicker than the surrounding mucosa, and in almost every instance project beyond and overhang the neighboring surface of the gut. The muscularis mucosae in the affected regions is pushed downward by the swelling of the submucosa. Between the muscle fibres that go to make up this layer there are considerable collections of fluids and great numbers of polymorphonuclear leucocytes; the muscle fibres themselves show no apparent alteration. In some situations the elastic tissue network of this layer does not take the stain in the usual way, and in the regions most diseased has apparently entirely disappeared.

The layer of the submucosa next to the muscularis mucosae is considerably swollen. This swelling is due to a mild degree of dilatation of the lymph channels and spaces, and, in addition, there is a considerable increase in the collagenous tissues found in the parts. In the lymph spaces there are many polymorphonuclear leucocytes and lymphoid cells, a few mucinoblasts, and a considerable number of plasma cells. Deeper portions of the mucosa are likewise to a certain degree swollen, but polymorphonuclear leucocytes are only found in this situation immediately around the bloodvessels; there are also present a few lymphoid cells and quite a number of most exquisite plasma cells. The collagenous tissues are here likewise somewhat increased.

No changes are found in either of the muscular coats, the subserous or serous coat.

#### EXPERIMENT IV. **Solution of sodium hydroxide. Duration, twenty-four hours.**

On January 7, 1901, there were injected into the rectum of a dog 10 c.c. of a solution of sodium hydroxide that corresponded in strength with the liquor potassae of the U. S. P. Exactly

twenty-four hours after the injection was given the animal was killed with chloroform, and an autopsy was at once made.

The large intestine contained fecal matter in its upper portion, but the lower half of the bowel was empty. On examination it was found that the mucosa of the lower part of the intestine was somewhat reddened and that the area presenting this change corresponded closely with the portion of the gut that was empty. The rugae were not so prominent as is usual, and the mucosa covering them did not appear more greatly affected than that overlying the neighboring portions of the gut. The walls of the bowel in this region were decidedly swollen.

On microscopic examination the mucosa of the intestine in the diseased area is found to be in a state of advanced necrosis. This layer, however, is not affected completely through in a uniform manner, for it may be distinctly divided into two separate and distinct portions—an upper, in which immediate death evidently followed the application of the alkali, and a deeper, in which the tissues did not suffer so severely, but have nevertheless undergone great alteration. The entire mucosa is greatly swollen, this applying especially to the deeper portion just referred to. Sections were made through the point at which the necrotic tissues came in contact with those that were normal, and the transition is found to be very abrupt; the normal tissues lie in direct contact with those that have undergone complete necrosis. In the diseased regions the superficial epithelium covering the mucosa has entirely disintegrated and sloughed away. The epithelial cells that line the mouths and necks of the crypts have likewise undergone complete degenerative change, but the granular debris resulting still remains in the lumina of the crypts to which the cells belonged. This granular debris is acidophilic throughout, and at no point are any distinct cellular elements to be made out within it; mixed with it there are here and there small particles of mucin, but this substance is almost entirely absent, and even that which is present does not stain in a perfectly normal way. The tissues lying between the remnants of the crypts are likewise in a state of advanced degenerative change, are uniformly acidophilic, and none of the structures present show any of the peculiarities that are characteristic of those that are normally found in the parts.

Between the superficial layer of the mucosa and the deeper one, in which the changes are not so greatly advanced, there is a thin stratum of tissue in which the nuclei of the cells of the interstitial substance stain deeply, and, in addition, the other tissues of the parts are decidedly basophilic, there being thus produced in sections properly prepared a dark line separating the two layers from each other.

Notwithstanding that the alterations in the deeper portions of the mucosa are not so marked as in the more superficial parts, the changes are still of a pronounced character. The crypts are widely separated from each other by masses of inflammatory exudate, and the cells lining them exhibit unmistakable evidences of degeneration. The outlines of the epithelial cells lining the lower portions of the bases of the crypts cannot, as a rule, be made out, and the cells are represented by masses of granular material in which nuclei may be occasionally found; the cells have so greatly swollen that the lumina of the crypts are in most instances entirely obliterated. Mucin formation is never observed in the cells of these crypts, but very rarely a small amount of this substance is found lying free in the lumina of the glands.

The elastic tissue basement membranes around these crypts do not, as a rule, stain well, but in properly prepared sections may be always discerned.

Between the crypts there are a great many polymorphonuclear leucocytes and considerable numbers of lymphoid cells, intermingled with which there are here and there a few red blood-corpuscles; in the fresh state the tissues evidently also contained large quantities of fluids. Mucinoblasts are never found in these situations. The fibrils of collagenous tissue stain in the usual way and do not appear to be altered to any extent. The smaller bloodvessels lying in these areas are considerably dilated and contain more than the usual number of polymorphonuclear leucocytes; in some instances they have ruptured.

The muscle fibres that go to make up the muscularis mucosae are widely separated from each other by collections of fluids and by great numbers of polymorphonuclear leucocytes. The individual muscle fibres, however, show no obvious alteration.

In the layer of the submucosa just beneath the muscularis



mucosa there are numbers of polymorphonuclear leucocytes, many lymphoid cells, and a few mucinoblasts, and, in addition, there are in the regions most affected great quantities of fibrin. The polymorphonuclear leucocytes and fibrin are not uncommonly found in the larger lymph channels. The bloodvessels in this region are usually dilated and are filled with blood. These changes in some instances extend completely through the submucosa, but in most situations the deeper portions of this layer, while showing changes similar to those just described, are by no means so greatly affected.

In many areas the circular muscular layer contains considerable quantities of fluids that push the fibres more or less apart, and small collections of polymorphonuclear leucocytes here and there; further than these there are no obvious alterations.

The longitudinal muscular layer shows to a less degree changes that are similar to those just described as occurring in the circular muscular layer; however, in most situations this coat is entirely normal.

The subserous and serous coats present no alteration.

#### EXPERIMENT V. **Solution of ammonium hydroxide. Duration, twenty-four hours.**

On January 15, 1901, 10 c.c. of a solution of ammonium hydroxide that corresponded in strength with the liquor potassæ of the U. S. P. were injected into the rectum of a medium-sized dog. Twenty-four hours later the animal was killed with chloroform, and an autopsy was at once made. The large intestine was filled with feces; the lower part of the gut was swollen, the rugæ numerous, and the mucosa was distinctly reddened, but there was no evidence of necrotic change.

On microscopic examination the superficial epithelium covering the mucosa is found to be entirely absent in the regions most affected, and not uncommonly the cells that lay in the mouths and necks of the crypts have entirely sloughed away. The superficial layer of the interglandular substance has likewise become necrotic and has disappeared. Generally the greater portions of the bodies and always the bases of the crypts are partially pre-



served, but even here the cells lining them show marked alterations. Between the deeper portions of the glands the supporting structures do not exhibit correspondingly extensive changes. Toward the free ends of these partially preserved crypts the epithelial cells show evidences of most pronounced degeneration, and have generally become completely necrotic; the granular debris that results from this disintegration of the epithelial cells is still found in the lumina of the crypts. Deeper down the cells are here and there fairly well preserved, but even in the basal portion of the glands they are swollen, irregular in form, and their outlines are very indistinct; the cells here, however, have nuclei that stain in the usual way. As is always the case in tissues that have been subjected to the action of alkalies, mucin formation is going on to a very limited degree in the epithelial cells of the affected glands, this substance, as a rule, being absent from their lumina. The elastic tissue basement membranes of the crypts do not take their specific stains in the usual way, and in many instances appear to have disappeared.

The tissues lying between the diseased crypts are considerably swollen, this being evidently due to dilatation of the small bloodvessels—which condition is very pronounced—collections in the parts of fluids, and to the infiltration of great numbers of polymorphonuclear leucocytes; in addition to the polymorphonuclear leucocytes, quite a number of lymphoid cells and a few plasma cells are found. Mucinoblasts nowhere occur in the interglandular substance. With the exception that the elastic tissue fibrils do not take the stain, no other alterations are perceptible in these structures. Around the bases of the glands changes of a similar kind are observed, but the swelling is not so great and the polymorphonuclear leucocytes are not so numerous; the bloodvessels, however, in this region are greatly dilated and are filled with blood.

The muscularis mucosæ is slightly swollen. Between the muscle fibres composing the layer fluids have here and there collected, and there are present quite a number of polymorphonuclear leucocytes and a few lymphoid cells.

In some areas the superficial portions of the submucosa are somewhat swollen and contain quite a number of polymorphonuclear

leucocytes, but the change is not very frequently observed. The bloodvessels, however, in this situation are usually dilated and filled with blood. In some of the larger lymph channels small quantities of fibrin are occasionally encountered, but this substance is by no means present to such an extent as is observed in inflammations induced by stronger alkaline substances.

The muscular, subserous, and serous coats are entirely unaltered.

### **Résumé of the Changes Produced as a Result of the Injection of Alkaline Solutions.**

**Very acute changes resulting from dilute liquor potassæ. (Twelve hours.)** On post-mortem examination the large intestine was found to be almost empty, and the mucous surface on its lower half was distinctly reddened.

On microscopic examination it was found that the superficial layer of epithelium has entirely disappeared. The outer half of the mucosa is in a semi-necrotic condition. All of the pre-existing structures in this area show advanced degenerative change. There have migrated into the parts, especially where they come in contact with the practically normal tissues that lie beneath, great numbers of polymorphonuclear leucocytes. There has also been a considerable amount of hemorrhage into the tissues. The structures in the deeper half of the mucosa, while presenting alteration, still preserve in a great measure the peculiarities that characterize them in health. Within the lumina of the crypts there are great quantities of mucin, but none of the epithelial cells contain the slightest trace of this substance.

The bloodvessels lying in the interstitial substance between the bodies of the glands are enormously dilated and filled with blood. Further than this no changes of any importance are found.

**Acute changes resulting from dilute liquor potassæ. (Twenty-four hours.)** When the large intestine was removed its surface was found to be covered with mucus. The mucosa of the lower half of the gut was of a grayish color, with small pinkish spots scattered over its surface.

On microscopic examination it was found that the changes present vary considerably in different parts of the specimens ex-

aminated. In some instances the destruction of the superficial epithelium and of the cells lining the mouths of the crypts has only occurred, while in other cases the entire mucosa has become completely necrotic. It is noteworthy that mucin is entirely absent from the epithelial cells lining the crypts in the affected areas.

Around the edges of the necrotic mucosa the tissues contain much effused blood, the result of the rupture of many blood-vessels in the diseased parts. The bloodvessels are all enormously dilated and filled with blood. The tissues contain polymorphonuclear leucocytes, plasma cells, lymphoid cells, large phagocytes, and numerous mucinoblasts.

The muscularis mucosæ is swollen and contains numerous polymorphonuclear leucocytes.

The tissues of the submucosa show a considerable degree of swelling, contain polymorphonuclear leucocytes, and, in many situations, fibrin. There were no changes of moment observed in the other coats of the intestine.

**Acute changes resulting from a dilute solution of sodium hydroxide. (Twenty-four hours.)** On examination the mucosa of the lower half of the large intestine is found to be decidedly reddened.

On microscopic examination the upper half of the mucosa was found to be in a state of advanced degeneration, and the remaining portion of this coat likewise showed marked alterations. In all instances the epithelial cells have shed off from the surface of the gut and from the mouths and necks of the crypts; the tissues intervening are entirely necrotic. In the bodies and bases of the crypts the epithelial cells are swollen, very irregular in form, and not uncommonly have shed off from their basement membranes; these cells never contain mucin within their protoplasm. This substance is not uncommonly found lying free in the lumina of the crypts. The lower portions of the glands are much compressed as a result of hemorrhage and of the accumulation of polymorphonuclear leucocytes and fluids in the surrounding tissues.

The interglandular substance of the deeper half of the mucosa is greatly swollen as a result of the presence of fluids. There are

found within the tissues many lymphoid cells, numerous polymorphonuclear leucocytes, and a few red blood-cells lying loose in the tissues. Mucinoblasts are entirely absent.

The muscularis mucosæ is swollen, and there are between the fibres numerous polymorphonuclear leucocytes.

The outer portion of the submucosa contains numerous lymphoid cells, many polymorphonuclear leucocytes, a few mucinoblasts, and considerable quantities of fibrin. These changes become less marked deeper down in the substance of this coat.

The muscular coats are swollen and contain here and there polymorphonuclear leucocytes.

**Acute changes resulting from ammonium hydroxide. (Twenty-four hours.)** At the post-mortem the wall of the gut was found to be considerably swollen and its mucosa reddened.

On microscopic examination the superficial epithelium is found to have everywhere desquamated, and changes of a similar kind are usually observed in the mouths and necks of the crypts. In the deeper portions of the glands the epithelial cells are swollen, irregular in form, and have frequently shed off from their basement membranes; none of these cells contain mucin, and there is but little of this substance found in the lumina of the crypts.

The interglandular tissues are distinctly swollen, this being the result of the dilatation of many of the smaller bloodvessels and from infiltration into the parts of great numbers of polymorphonuclear leucocytes. Mucinoblasts are always absent.

The bloodvessels of the muscularis mucosæ and of the neighboring layer of the submucosa are distinctly dilated and are filled with blood. Many polymorphonuclear leucocytes are found in the interspaces of these tissues.

**Chronic changes resulting from liquor potassæ. (Twenty days.)** At the necropsy the wall of the gut was found considerably swollen and its mucous surface decidedly reddened. There were no macroscopic evidences of ulceration.

On microscopic examination there were found numerous small ulcers scattered over the surface of the intestine, and these lesions are, as a rule, sharply marked off from the surrounding practically normal structures. In the diseased areas the tissues that constituted the mucosa are found entirely necrotic in almost all

cases, and, taking their places, is a granular debris, intermingled with which there are multitudes of polymorphonuclear leucocytes. In those instances where any parts of the glands remain in the affected areas the epithelial cells lining them show evidences of catarrhal change.

In the vicinity of the ulcers just described the muscle fibres of the muscularis mucosæ are pushed apart by great numbers of polymorphonuclear leucocytes and by the accumulation of fluids.

The tissues of the submucosa that lie immediately beneath the lesions just referred to are swollen and contain great numbers of polymorphonuclear leucocytes, many lymphoid cells, mucinoblasts, and plasma cells. Considerable new formation of collagenous tissue has occurred in these parts.

## CHAPTER III.

### EXPERIMENTS TO DETERMINE THE EFFECTS PRODUCED ON THE LARGE INTESTINES OF DOGS AS A RESULT OF THE INJECTION OF ACIDS.

#### EXPERIMENT I. Dilute sulphuric acid. Duration, twelve hours.

ON February 26, 1901, 10 c.c. of a solution of sulphuric acid were injected into the rectum of a dog; this solution consisted of 1 part of the acid to 189 parts of water. Twelve hours later the animal was killed with chloroform, and an autopsy was at once made.

The entire large intestine was found to be practically empty. The mucosa of the lower half of the bowel was reddened; the discoloration was uniform in the affected region. In the same part of the bowel there were numerous transverse rugae. The walls of the lower half of the gut were decidedly swollen.

On microscopic examination it is found that the surface layer of epithelial cells has entirely shed off from the mucosa of the intestine, and not uncommonly changes of a like kind have occurred in the mouths and necks of the crypts. These shed-off cells may be sometimes seen lying along the surface of the mucosa; they are swollen and irregular in form, and their protoplasm is, as a rule, decidedly basophilic throughout, this being apparently the result of the breaking up of the nuclei, and the diffusion of their chromatin throughout the protoplasm of the cells. The cells that line the bodies and basal portions of the crypts have occasionally desquamated and present changes in every way similar to those that have been described as occurring in the surface cells; but more commonly they still remain attached to their basement membranes, and exhibit no alteration further than that their protoplasm is unusually basophilic. Lying between these

cells polymorphonuclear leucocytes are not uncommonly encountered, and in some instances they have collected in considerable numbers in the lumina of the glands. The crypts are considerably compressed as the result of the accumulation of cells and fluids in the surrounding tissue. The basement membranes of the diseased crypts show practically no alteration.

Between the mouths and necks of the crypts the bloodvessels have universally ruptured and there lie between the glands great masses of blood. Polymorphonuclear leucocytes have also migrated into the parts in considerable numbers, and in some situations are quite as numerous as the red blood-corpuscles. The pre-existing cells of these tissues are still present, the mucinoblasts appearing to have even increased in number. The collagenous tissue fibrils are here so obscured by the effused blood that they can no longer be distinguished with certainty. As the deeper portions of the glands are approached these changes in the interglandular substance gradually decreases in severity until around the basal portions of the crypts there are no changes other than that there are quite a number of polymorphonuclear leucocytes intermingled with the pre-existing cells of the part.

The muscularis mucosæ shows no alteration except that there are numerous polymorphonuclear leucocytes lying between the fibres composing the coat.

The layer of the submucosa that lies in the vicinity of the muscularis mucosæ contains numerous polymorphonuclear leucocytes and an unusual number of mucinoblasts. In this region the smaller bloodvessels are decidedly dilated, but further than this there are no alterations. The outer portions of the submucosa are normal.

The remaining coats of the intestine show no change.

#### EXPERIMENT II. Dilute sulphuric acid. Duration, twenty-four hours.

To a dog weighing 7 kg., 10 c.c. of dilute sulphuric acid were administered by the rectum on November 13, 1900; the liquid that was given consisted of 1 part of pure acid to 89 parts of distilled water, this being the dilution necessary to give a solution



that will exactly neutralize the liquor potassæ of the U. S. P., volume for volume. Twenty-four hours after the drug was given the animal was killed with chloroform. On examination the mucosa of the large intestine showed slight redness in its lower portions, the change being as usual most marked on the tops of the rugæ; this alteration is not uniform even in the lower part of the bowel.

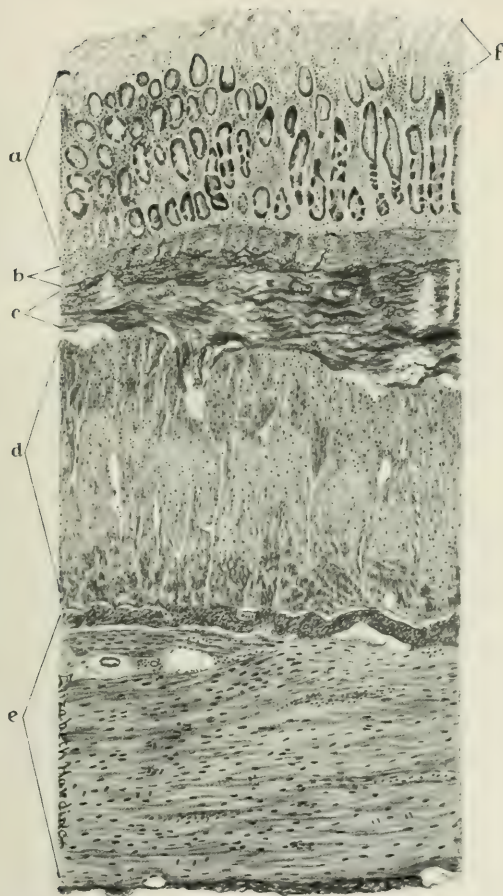
On microscopic examination with a low power very extensive changes are at once apparent in the mucosa, the muscularis mucosæ, and the submucosa. The surface layer of epithelial cells covering the mucous membrane has been completely destroyed, and the epithelial cells in the mouths and necks of the glands and the structures intervening between them are entirely necrotic. The tissues lying along the surface of the gut are uniformly acidophilic, the nuclei never taking even the most powerful basic stains. These structures are for the most part finely granular, and along the surface, in most situations, do not present any of the morphologic peculiarities that characterize the normal tissues of the parts.

Somewhat deeper down the tissues, while still being practically entirely acidophilic, begin to exhibit in their morphology a certain resemblance to those normally found in the parts. The epithelial cells lining the crypts are swollen, exceedingly irregular in form, and acidophilic throughout, and, although attached to their basement membranes, the coverings of their free ends have in most instances ruptured, and the cellular contents have oftentimes been discharged in irregular masses into the lumina of the crypts. In many of these cells small rounded or oval masses of mucin are found, and it is especially noteworthy that they preserve their form and staining peculiarities, however degenerate the surrounding parts of the cells may be.

Between the crypts in these situations the tissues are considerably swollen, though by no means to such a degree as is often observed in other experimental lesions. The bands of elastic tissue stain fairly well, even for quite a distance into the masses of necrotic material that lie on the surface, and have suffered much less than the neighboring fibres of collagenous tissue. In the dilated lymph spaces there are numerous red blood cells and



# PLATE VIII.



Specimen from the lower portion of the large intestine of a dog into which a dilute solution of sulphuric acid had been injected twenty-four hours before the tissues were removed from the animal's body. The specimen was fixed in Bensley's solution and stained by the method of Van Gieson. Beck  $\frac{1}{2}$  inch, Oc. 1 inch. *a.* Mucosa, the outer portion of which (*f*) is entirely necrotic, and deeper down there is much catarrhal change in the glands, and the intervening tissues are swollen, and contain many polymorphonuclear leucocytes and free red blood cells; the polymorphonuclear leucocytes are particularly numerous where the necrotic tissues join those not so much altered. *b.* Swollen muscularis mucosae, in which there are many polymorphonuclear leucocytes. *c.* Submucosa containing here and there minute collections of polymorphonuclear leucocytes. *d.* Circular muscular layer. *e.* Longitudinal muscular layer. (Exp. II.)



quite a number of polymorphonuclear leucocytes—these in the fresh state, having evidently been surrounded by considerable collections of fluids. These blood cells often stain in a practically normal manner in regions so near the surface that the pre-existing structures are entirely degenerate, and it is plain that they were effused into the parts after the maximum deleterious action of the acid had passed away.

Below the areas of actual necrosis the epithelial cells lining the crypts show marked alterations; they are swollen, irregular in form, and have usually shed off from their basement membranes; the nuclei, however, are practically always normal in appearance and stain in the usual way. These cells contain quantities of mucin that is often present as round or oval masses within the cells, or, even more commonly, diffusely scattered throughout their protoplasm. Considerable quantities of free mucin are also found in the lumina of the crypts in these situations. The cells lining the bases of the crypts have likewise shed off from their basement membranes, and are usually swollen and irregular in form, but both their nuclei and their protoplasm stain in the usual manner. Even here mucin formation is frequently observed in the cells, thus indicating that an increased amount of this substance is being produced. Mixed with the shed-off cells there are frequently found collections of polymorphonuclear leucocytes that have evidently made their way through the basement membranes into the lumina of the crypts. The basement membranes of the bodies and bases of the glands appear entirely normal and stain in the usual way.

The interstitial tissues lying between the crypts immediately beneath the area of necrosis show marked alteration. The collagenous fibres are swollen and take their specific stains poorly, while the neighboring elastic tissue fibrils appear in every way normal. The lymph spaces are considerably dilated and are filled with many red cells and multitudes of polymorphonuclear leucocytes; in these situations there are found here and there lymphoid cells and an occasional plasma or connective tissue cell, but the blood cells so largely predominate that they entirely overshadow all other cellular bodies present. It seems probable that the walls of the bloodvessels have been completely destroyed in these areas,

as no distinct bloodvessels can be made out. Mucinoblasts are entirely absent from these tissues. Similar changes are observed around the bases of the crypts, the only difference being that the swelling is not so marked and the number of polymorphonuclear leucocytes is somewhat less.

The muscular fibres composing the muscularis mucosae are very generally more or less separated from each other by fluids that have accumulated between them, and polymorphonuclear leucocytes are very frequently present in the dilated lymph spaces. The muscle fibres composing this layer show no change.

The layer of the submucosa that is immediately beneath the muscularis mucosae shows considerable alteration. The lymph spaces are dilated, and were evidently filled with fluids in the fresh state; within these spaces small collections of fibrin occasionally occur. In these situations there are found considerable numbers of polymorphonuclear leucocytes, a few lymphoid, plasma, and connective tissue cells; small collections of red blood cells are not infrequently present. The bloodvessels are in many instances dilated, and polymorphonuclear leucocytes are frequently seen collected around and lying attached to their inner coats. Both collagenous and elastic tissues stain in the usual way, and both appear entirely normal. The deeper layers of the submucosa show similar changes, but they are by no means so marked; the tissues of this coat that border upon the circular muscular layer are practically normal. It is a curious fact that the mucinoblasts have entirely disappeared from this layer also.

No changes are found either in the muscular, subserous, or serous coats.

### EXPERIMENT III. Dilute sulphuric acid. Duration, twenty days.

On December 11, 1900, a dog was given by the rectum 10 c.c. of a solution of sulphuric acid composed of 89 parts of water and 1 part of acid; from this the animal suffered no apparent ill effect. On December 14th the injection was repeated. On the following day the animal was observed to pass much mucus, mixed with blood, and he was evidently quite ill. On December 17th 10 c.c.

of the acid solution were again injected. The dog continued to suffer with diarrhœa, and became so weak that it was thought best not to give another dose of the acid until December 23d, following which he became still weaker. The injection was repeated on December 28th. On December 31st the dog was killed with chloroform, and an autopsy was at once made. The animal was much emaciated, even more so than the one that had received the injections of liquor potassæ on the corresponding dates. On examination no changes were found except in the large intestine; this viscus was entirely empty, and its walls seemed to be about twice the usual thickness. The rugæ on its surface were not so prominent as is usually the case. The mucosa was of a pinkish-gray color, with here and there small spots that were of a light rose-red hue. The appearances are those that would indicate a superficial necrosis of the mucous layer, but there is no evidence of deep ulceration into the wall of the gut.

On microscopic examination it was found that the mucosa, in those areas with which the acid came in contact, had entirely sloughed away. The destruction in some cases does not extend below the muscularis mucosæ, but in the majority of instances the pathologic process has gone deeper, and has involved to a greater or less extent the upper layer of the submucosa. In the diseased region the surface of the gut is made up by masses of polymorphonuclear leucocytes, intermingled with which there are found many lymphoid cells and a considerable amount of granular debris. Higher up the gut its surface no longer presents this necrotic change, but the normal mucosa is again found. Where these two areas join the mucous layer begins abruptly. Here the layer of epithelial cells covering the mucosa dips suddenly downward to the ulcerated surface and has made a feeble sort of an effort to grow over it for a short distance; these epithelial cells appear entirely normal except just at the edges of the necrotic areas, where they are somewhat smaller and more irregular in form than is usual. The cells lining the neighboring crypts contain considerable quantities of mucin, but present no other obvious alteration. The tissues lying between the crypts are somewhat swollen, and the bloodvessels are in many instances slightly dilated, but further than this no change is apparent. Underlying the tissues

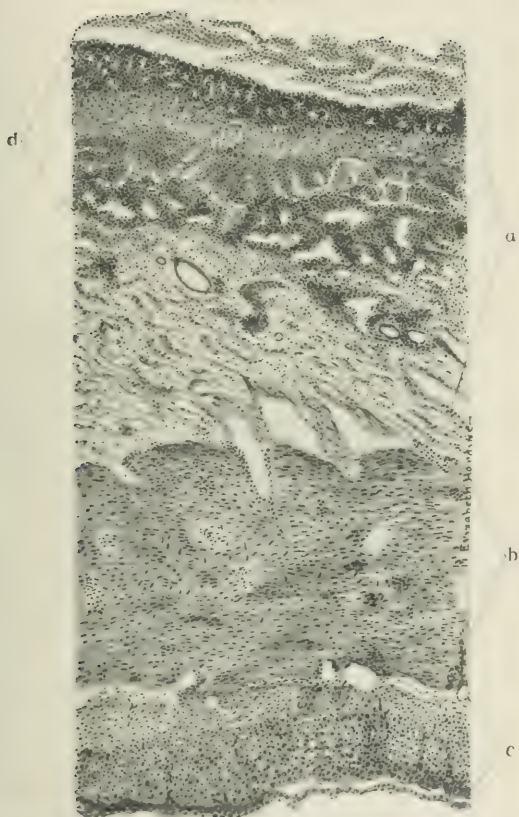
composing the surface of the ulcerated portion of the gut there is an extensive layer containing remnants of the original fibrous structures, a few polymorphonuclear leucocytes and lymphoid cells, and large quantities of fibrin; the fibrin is present to such a degree that in properly stained specimens the tissues appear to be almost entirely made up of this substance. Still deeper down the tissues are much swollen and contain great numbers of plasma cells that very generally are in the process of secreting fibrous tissue; in addition to these there are many lymphoid cells, a few polymorphonuclear leucocytes, and a small number of mucinoblasts. The tissues lying in this area are for the most part entirely degenerate and do not take their specific dyes, but the fibres of white fibrous tissue, although greatly swollen, react to stains in the usual way. The bloodvessels are in most instances dilated, and, near the fibrin layer above referred to, are frequently thrombosed. The muscular walls of these vessels in many instances show practically no alteration, but in others the fibres have lost their identity and have been transformed into solid masses of hyaline material that react strongly to acid stains. Under all conditions, and especially in the latter instances, the elastic tissue fibrils lying in the walls of the vessels show pronounced degenerative change and usually fail to stain. The epithelial cells lining the lymph channels are greatly swollen, and the lumina of these vessels are frequently filled up with desquamated epithelial cells, polymorphonuclear leucocytes, lymphoid cells, and granular debris.

The muscular coats of the gut show comparatively little alteration, but lying between the fibres of the circular muscular layer small collections of polymorphonuclear leucocytes are not uncommonly encountered, and in the fibrous septa between the bundles of the muscle fibres minute groups of lymphoid cells and plasma cells are frequently found. Mucinoblasts are also quite commonly observed in the circular muscular layer.

The longitudinal muscular layer is practically normal.

The subserous and serous coats show no alteration.

PLATE IX.



Specimen from the lower portion of the large intestine of a dog into which dilute sulphuric acid was injected at intervals for twenty days previous to the removal of the tissues from the animal's body. The tissues were fixed in Bensley's solution and stained with hemalum and eosin. Beck  $\frac{1}{4}$  inch, Oc. 1 inch. *a.* Submucosa, the surface of which is covered by a granular debris, and lower down the tissues contain enormous numbers of polymorphonuclear leucocytes and lymphoid cells. *d.* *b.* Circular muscular layer. *c.* Longitudinal muscular layer. (Exp. III.)





**EXPERIMENT IV. Dilute nitric acid. Duration, twenty-four hours.**

On January 7, 1901, there were injected into the rectum of a dog 10 c.c. of a watery solution of nitric acid that corresponded in strength to the sulphuric acid solution employed in Experiments II. and III. In exactly twenty-four hours the animal was killed with chloroform, and an autopsy was at once made. When the large intestine was opened its upper half was found to contain fecal matter; the lower portion was practically empty. The walls of the lower half of the gut were swollen and the rugae were much less prominent than usual. In this situation the mucosa was pinkish-gray in color, with here and there small areas that were decidedly redder than the surrounding parts. At a point about three inches from the rectum, which corresponds to the place where the end of the syringe rested while the injections were being made, the mucosa was evidently necrotic and presented the appearance of superficial ulceration.

On microscopic examination it is found that in those areas where the acid came directly in contact with the mucosa the upper layer of this coat is entirely necrotic, and is beginning to slough off in many situations. With the exception that the superficial layer of the epithelial cells is here absent, the different morphologic elements that go to make up the mucous layer are found to be present, and occupy the relative position in which they occur in health. The epithelial cells in the mouths and necks of the crypts have entirely disintegrated, and the granular debris that results stains uniformly with acid dyes. However, scattered through these masses, particles of mucin are not uncommonly encountered that in some instances often preserve their normal form, and in all cases stain in the usual way. Somewhat lower down, but still within the mass of necrotic tissue, the epithelial cells do not show such marked evidences of degenerative change, but even here their outlines are ill-defined, the cells appear shorter than normal, and their nuclei often fail to stain; the mucin particles within the cells show no alteration in either form or staining reactions. The elastic tissue basement membranes surrounding the crypts are fairly well-preserved, and stain in many instances

outward to the free ends of the crypts. In the superficial portions of the sloughing tissues the interstitial structures are totally acidophilic, but even here swollen bands of collagenous tissue may be readily made out. Between the crypts in the lower portion of these masses there are multitudes of polymorphonuclear leucocytes, these occurring in such numbers that they practically replace all other tissues that were previously present, and push the bodies of the crypts widely apart.

Frequently the necrotic portions of the mucosa still remain attached to the more or less normal tissues that lie beneath, but under these circumstances the changes occurring in the dead tissues are in every way similar to those just described.

The only parts of the mucous layer that retain in any way their normal peculiarities are the basal portions of the glands and the intervening structures, but even here the epithelial cells are usually swollen and irregular in form, and quantities of them have desquamated in all instances and lie loosely in the lumina of the crypts. Intermingled with these shed-off epithelial cells there are also numerous polymorphonuclear leucocytes, these being present in such numbers oftentimes that they completely fill the lumina of the crypts. Neither the polymorphonuclear leucocytes nor the epithelial cells, however, show any alteration in their staining peculiarities. The basement membranes of the crypts stain in the usual way.

The tissues that lie between the lower portions of the crypts and around their bases are very greatly swollen and contain, in addition to the fluids that were evidently present to a considerable extent, great numbers of polymorphonuclear leucocytes, a few mucinoblasts, and a few plasma cells. Occasionally dilated bloodvessels are found in these areas, but they are by no means commonly present. In some instances they have evidently ruptured, and under these circumstances small hemorrhages are found in the surrounding tissues. The collagenous tissues are fairly well-preserved, though the fibrils usually appear slightly swollen.

The outer layers of the muscularis mucosae are somewhat swollen, and there are numerous polymorphonuclear leucocytes lying between the muscle fibres.

The deeper portions of this coat are practically normal.

The submucosa shows no change with the exception that the bloodvessels, especially those lying immediately beneath the muscularis mucosae, are greatly dilated and are filled with blood; around these bloodvessels a few polymorphonuclear leucocytes are sometimes found.

The other coats of the intestine are entirely normal.

#### EXPERIMENT V. Dilute acetic acid. Duration, twenty-four hours.

Ten c.c. of a solution of acetic acid, corresponding in strength to the acid solutions used in Experiments II., III., and IV., were injected into the large intestine of a dog on January 18, 1901. Twenty-four hours later the animal was killed with chloroform, and an autopsy was at once made. On examination the large intestine was found to be filled with fecal matter. The walls of the lower half of the gut were swollen and the mucosa was quite red. The rugae were numerous and prominent; the mucosa covering these elevations was no redder than the neighboring surface of the bowel.

On microscopic examination it is found that the superficial layer of surface epithelium has been completely eroded away in those parts with which the acid came in direct contact, and in some situations the tissues immediately beneath have likewise become necrotic and have sloughed away. The necrosis has in some situations extended down into the necks of the crypts, but in most instances the process has only involved the epithelial cells lying at the margins of the mouths of the glands. However, more or less alteration is always found in the cells in these situations, for they are swollen, irregular in form, and their protoplasm is decidedly granular; in many instances they have shed off from their basement membranes. These changes sometimes extend downward into the necks of the crypts, but never go deeper, the cells lining the bodies and bases of the glands being entirely normal. No mucin is found in any of the diseased epithelial cells, and this substance is evidently being produced in much smaller quantities than normal in the tissues that lie beneath, they con-

taining only here and there traces within their protoplasm. The elastic tissue basement membranes upon which the diseased epithelial cells lie appear and stain in a perfectly normal manner.

The tissues intervening between the mouths and necks of the glands are greatly swollen, this being due to enormous dilatation of the smaller bloodvessels lying in the parts, to the accumulation of quantities of fluids in the tissues, and likewise to the presence of many polymorphonuclear leucocytes; in addition to the above-named cellular elements, a few lymphoid and a small number of plasma cells are present. Mucinoblasts are never observed in the diseased tissues. The collagenous and elastic tissue fibrils stain in a perfectly normal manner, even where the alterations are most pronounced. Changes similar to those just described, though much less marked, are found in the tissues intervening between the bodies of the crypts and occasionally even so low down as between and beneath the bases of these glands; on the whole, however, the alterations may be said to be confined to the upper half of the mucosa.

No changes are found in any of the other coats of the intestine.

### Résumé of the Changes Resulting from Acids.

**Dilute sulphuric acid. Very acute. (Twelve hours.)** At the post-mortem examination the mucosa of the lower half of the large intestine was found considerably reddened and its walls were decidedly swollen.

Microscopic examination shows that the superficial epithelium has entirely desquamated, and that the cells of the mouths and necks of the crypts exhibit catarrhal alteration. In some instances these changes extend down into the bodies of the glands. Between the epithelial cells in the deeper portions of the crypts there are quite a number of polymorphonuclear leucocytes; in some instances these have collected in considerable numbers in the lumina of the crypts. The interglandular tissues are considerably swollen as a result of the effused blood, and polymorphonuclear leucocytes have migrated into the part in great numbers.

The muscularis mucosæ is somewhat swollen. In the inter-

spaces of the tissues there are here and there quite a number of polymorphonuclear leucocytes.

The layer of the submucosa lying next to the muscularis mucosæ contains numerous dilated bloodvessels. There are many polymorphonuclear leucocytes in the interspaces of these tissues.

**Dilute sulphuric acid. Acute. (Twenty-four hours.)** On post-mortem examination the lower half of the intestine was found decidedly reddened.

On microscopic examination the epithelium that covered the surface of the mucosa and that that lined the mouths and necks of the crypts is found absent. The interglandular tissues immediately along the surface are entirely necrotic. The epithelial cells in the bodies of the crypts show decided catarrhal change. Polymorphonuclear leucocytes have frequently penetrated between these cells and lie in considerable numbers in the lumina of the crypts. The interglandular tissues are here greatly swollen as a result of the presence of much hemorrhage and of great numbers of polymorphonuclear leucocytes. The pre-existing structures, with the exception of the elastic tissue fibrils, have entirely disappeared in these situations. In the bases of the crypts the epithelial cells are sometimes catarrhal, and there is much mucin formation going on within them.

The muscularis mucosæ is swollen and contains in its interspaces numerous polymorphonuclear leucocytes.

The more superficial layers of the submucosa are swollen as a result of the presence of fluids and of great numbers of polymorphonuclear leucocytes.

**Dilute nitric acid. Acute. (Twenty-four hours.)** The mucosa of the lower half of the large intestine was found to be reddened and at some points necrotic on post-mortem examination. In the same situations the walls of the gut were distinctly swollen.

On microscopic examination the epithelium that lined the surface of the intestine and that that covered the mouths and necks of the glands is found to have entirely desquamated. The interglandular substance at these points is entirely necrotic. In the deeper portion of the necrotic tissues there are multitudes of polymorphonuclear leucocytes.

In the basal portions of the glands the epithelial cells have universally desquamated, but preserve their form and staining reaction in an almost normal way. Intermingled with these cells there are great numbers of polymorphonuclear leucocytes. The interglandular tissues of the basal portions of the crypts are much swollen; this is the result of the presence of great quantities of liquids and quite an amount of hemorrhage. Polymorphonuclear leucocytes are abundantly present in these tissues. The pre-existing collagenous tissues stain very poorly, but the elastin presents practically no alteration.

The muscularis mucosae is swollen. Between its fibrils there are numerous polymorphonuclear leucocytes.

The bloodvessels of the more superficial portions of the submucosa are considerably dilated, and the interspaces of the tissues contain numerous polymorphonuclear leucocytes.

**Dilute acetic acid. Acute. (Twenty-four hours.)** At the autopsy the lower half of the large intestine was found to be swollen and its mucosa somewhat reddened.

The epithelial cells that covered the surface of the intestine have entirely shed off, and those that normally line the mouths and necks of the crypts have in some instances undergone a similar change. The cells in the lower portions of the crypts are entirely normal. The elastic tissue basement membranes are in all situations normal. The interglandular tissues are considerably swollen as a result of the dilatation of the bloodvessels of the part and of the accumulations in the lymph spaces of great quantities of fluids. These structures contain enormous numbers of polymorphonuclear leucocytes. The pre-existing collagenous and elastic tissues stain normally. These changes are confined almost entirely to the outer half of the mucosa, there being but little alteration in the deeper portion of this coat.

**Dilute sulphuric acid. Chronic. (Twenty days.)** Some time before the dog died he became considerably emaciated. At the autopsy the walls of the lower half of the large intestine were found to be considerably thickened, and the mucous surface was of a pinkish-gray color, with red spots scattered here and there upon its surface.

On microscopic examination the mucosa is found to be entirely

absent, and the ulceration has extended in many instances even through the muscularis mucosæ. The surface of these ulcers consists of a granular débris, intermingled with which many polymorphonuclear leucocytes and lymphoid cells are found. Specimens were examined at the point where the diseased part of the bowel joined the normal portion that lay in the upper part of the gut. It was found that the lesions at this point begin abruptly, and that epithelial cells have grown down from the normal mucosa over the edges of the ulcerated surface. Beneath the floors of the ulcers there are the remains of the original tissues of the part, intermingled with which there are many polymorphonuclear leucocytes and lymphoid cells and an enormous amount of fibrin. At some distance below the surface of the ulcers there are great numbers of plasma cells, and, as a consequence, much fibrous tissue is being formed in these parts. The vessels lying in the tissues below the surface of the ulcers are dilated and are often thrombosed. The walls of many of these vessels are hyaline.



## CHAPTER IV.

### EXPERIMENTS TO DETERMINE THE EFFECTS PRODUCED ON THE LARGE INTESTINES OF DOGS BY THE INJECTION OF SOLUTIONS OF NITRATE OF SILVER.

#### EXPERIMENT I. **Ten per cent. solution of nitrate of silver.** **Duration, twenty-four hours.**

ON February 6, 1901, 10 c.c. of a 10 per cent. solution of silver nitrate were injected into the large intestine of a medium-sized dog, he having previously received a large dose of morphine. Following the injection the animal exhibited no evidence of illness, but as he was killed just twenty-four hours after the drug was administered it was quite possible that the morphine prevented the development of the usual symptoms that result when the intestinal mucosa is subjected to irritation.

On post-mortem examination the lower half of the large intestine was found to contain a small quantity of fecal matter, and the mucosa covering this part of the bowel was uniformly quite red. The transverse rugæ were prominent in this situation, but their apices appeared no redder than the surrounding surfaces. There were at no points evidence of ulceration.

On microscopic examination the superficial layer of epithelium that covered the mucous surface in health was found to be eroded in the regions most affected, and along the surface of the mucosa there were found many swollen cells and much granular detritus. The epithelial cells that lined the mouths of the crypts show a marked catarrhal change, they being swollen, irregular in form, and have in most instances desquamated. It is noteworthy that these cells contain no mucin, and neither is this substance found in any part of the glands or on the surface of the intestine in the area most affected. The cells in the necks of the crypts are oftentimes swollen and have frequently shed off from their basement membranes, though these changes are by no means so marked as are



found in the mouths of the glands. The epithelial cells lining the bodies of the crypts show slight catarrhal changes in some instances, but, further than this, and that they never contain mucin, no further alterations are observed. The epithelium lining the bases of the crypts show no change. It should be noted that the lumina of the crypts in these situations are always much diminished, owing to the fact that the exudate in the surrounding interglandular substance has frequently caused considerable compression of the crypts, they being in many instances not more than  $30\mu$  from basement membrane to basement membrane in diameter. The basement membranes of the crypts do not stain well toward the free surface of the bowel, but deeper down around the basal portions of the crypts they show but little change.

The free surface of the interglandular tissues that have been denuded as a result of the shedding off of the surface epithelium shows slight evidence of necrotic change. The cells that lay in these situations have generally become necrotic, and the collagenous tissue fibrils are swollen and are oftentimes granular; these structures take the acid stains with much intensity. Immediately beneath the surface the interglandular tissues are very greatly swollen as a result of the accumulation of much fluid in the parts, from numerous hemorrhages, and in a considerable degree as an outcome of the emigration into the parts of multitudes of polymorphonuclear leucocytes. As would naturally be expected, the bloodvessels are also much dilated and are distended with blood. In addition to these extraneous substances there are the usual number of lymphoid cells and many pseudoplasma cells, the latter appearing to be present in greater numbers than is usual in health. It is noteworthy that mucinoblasts have entirely disappeared from the tissues most affected. While these changes are most pronounced toward the free surface of the mucosa, they show but little diminution in intensity as the deeper portions of this layer are approached, the alterations being almost as severe around the basal portions of the crypts as in the more superficial portions. It should also be noted that changes of a similar kind, though not quite so intense, are present between the crypts in many situations where the epithelial structures covering the surface of the gut and those lining the crypts have practically remained entirely

normal. It would therefore seem that nitrate of silver or the acid that results from its decomposition is absorbed into the deeper tissues, where its greatest action is exerted.

The fibres of the muscularis mucosae appear normal, though they are universally separated from each other by more or less fluid in which there are often polymorphonuclear leucocytes. The coat, as a whole, is therefore decidedly thickened. The elastic tissue network of this layer seems to have suffered no change.

The submucosa is decidedly thickened beneath those areas where the changes in the mucosa are most marked, this being due to the accumulation of liquids in the parts, to the dilatation of the bloodvessels, and to the presence in the tissues of great numbers of polymorphonuclear leucocytes. There are also found many more than the usual number of lymphoid cells in these tissues, but the mucinoblasts have entirely disappeared. The bands of collagenous tissues, especially those lying next to the submucosa, are distinctly swollen and appear somewhat granular, and the elastic tissues do not take their specific stains with quite the usual intensity. The connective tissue cells seem to have entirely disappeared. The number of dilated bloodvessels in this layer is much greater than the writer has ever observed in any other experimental lesion of the intestine; the vessels are invariably filled with blood. The lymph nodes—which are very frequent in the submucosa—are distinctly swollen, their bloodvessels are dilated, and they contain in addition to an increased number of lymphoid cells a great many polymorphonuclear leucocytes.

Notwithstanding that the changes are so marked in the submucosa, further than here and there a slight dilatation of the vessels, no changes are observed in the muscular coats.

The subserous and serous coats are normal.

#### EXPERIMENT II. Dilute solution of silver nitrate. Duration, eighteen days.

On February 6, 1901, 2 c.c. of a 10 per cent. aqueous solution of nitrate of silver were injected into the rectum of a rather large dog. The injections were repeated on the 8th, 10th, 12th, 14th, 16th, 18th, 20th, and 22d of February. During this period the

dog remained apparently healthy, with the exception only that the stools, which were not particularly numerous, contained more or less bloody mucus. On February 24, 1901, the animal was killed with chloroform, and an autopsy was at once made.

The mucosa of the lower half of the large intestine was found to be somewhat redder than normal, with here and there over its surface bright blood-red spots. The transverse rugæ were quite numerous in the area showing the most marked change, but the mucosa covering the apices of these elevations was no redder than that surrounding. The walls of the gut were decidedly swollen in the affected region.

On microscopic examination it is found that the epithelial structures of the mucosa of the intestine have suffered comparatively little, but there are most pronounced changes in the interglandular tissues of the sections examined. Although the epithelial cells show no marked alteration, it is universally the case that they stain somewhat more intensely with basic dyes than is usual, and there are within their protoplasm no structures that react in a frank manner to the specific stains for mucin; with Mayer's muchæmatein the cells sometimes stain throughout of a reddish-purple color; but, while there is a suggestion of mucin in the tint imparted to them, the reaction is not so pronounced as to warrant the assertion that they really contain this substance. The changes in the interstitial substance consist in a dilatation of the lymphatics of the tissues, this occurring in an especially marked manner near the surface of the mucosa, and the accumulation in the parts of enormous numbers of plasma cells; there are, in addition, a few polymorphonuclear leucocytes, quite a number of lymphoid cells, and many mucinoblasts. In the regions where the swelling is most marked the collagenous tissue fibrils are distinctly swollen and take the stain very poorly. On the other hand, the elastic tissues appear to be in every particular normal. Around the basal portions of the crypts mucin is frequently present in considerable quantity; it lies loosely in the tissues, and probably is the result of the disintegration of the mucinoblasts that are very numerous in these areas. The bloodvessels of the interglandular substance shows comparatively no change.

The muscularis mucosæ is decidedly swollen, its fibres often

appear somewhat larger than usual, and their protoplasm is distinctly granular. Between the muscle fibres there are a few polymorphonuclear leucocytes and lymphoid cells in addition to the fluid that is present in the lymph spaces in considerable quantity.

The layers of the submucosa lying next to the muscularis mucosae contain numerous plasma cells, and there appears to be a certain amount of fibrous tissue formation going on in this region. There are also in these tissues great numbers of large mucinoblasts, and here and there are found small collections of polymorphonuclear leucocytes and lymphoid cells.

As the circular muscular coat is approached the changes become less and less pronounced until those tissues that lie in contact with this layer appear perfectly normal. The bloodvessels of the submucosa present no alterations, with the exception that their muscular walls appear swollen and the fibres granular.

No changes are observed in either the circular or longitudinal muscular coats other than that the fibres composing these layers appear granular, and their outlines are ill-defined. The elastic tissue stroma of these coats, however, presents no alteration.

The subserous and serous coats show no change.

In some situations the alterations have been more pronounced; the epithelial cells lining the surface of the mucosa have shed off and there are slight catarrhal changes in the mouths of the crypts. The interglandular substance and deeper coats of the bowel present appearances in every way similar to those that have just been described as occurring more generally, though it is possible that the changes in the former instances may be somewhat more severe. It is noteworthy that where the superficial epithelial layer has desquamated the interglandular substance lying beneath has appeared in a measure to collapse, this doubtless being due to the fact that under these circumstances the fluids that were contained in the part have found ready exit onto the free surface of the intestine.

In some situations the mucosa has suffered even more greatly, and a large part of its substance has sloughed away. These alterations, however, must have resulted from some of the earlier injections, for reparative changes have gone on to a considerable degree in the areas involved. Over the parts affected a new coating of

epithelial cells has grown; these cells are fairly well-developed and exhibit in their histology the peculiarities that characterize ordinary surface epithelium, with the exception only that they never contain mucin. They do not lie upon a basement membrane, but are in direct contact with the tissues beneath. There are here and there vestiges of the original glandular structures of the parts remaining; these remnants of the glands are, as would be expected, not so tall as the crypts found in the normal mucosa, but their circumference is often two or three times as great. In some cases the openings of these crypts appear to have been occluded, and there have resulted cystic dilatations of the glands; the contents of these cysts consist of desquamated epithelial cells and granular debris in which no mucin is found. It may be remarked, however, that the epithelial cells lining both the cysts and the dilated crypts do not, as a rule, present any evidences of catarrhal change, but they stain somewhat more deeply than do the cells in health. Between these distorted crypts there is an interglandular substance composed of newly-formed fibrous tissue, in the interspaces of which there are enormous numbers of plasma cells, many lymphoid cells and mucinoblasts, and a few polymorphonuclear leucocytes; red blood-corpuscles are sometimes found lying loosely in these tissues, this having evidently resulted from the rupture of the embryonic bloodvessels that have penetrated the parts.

Beneath these areas the muscularis mucosæ, submucosa, and circular muscular coats present changes in every way similar to those that occur in other parts of the diseased intestine.

From the foregoing it is apparent that the changes produced by nitrate of silver resemble very closely those caused by nitric acid.

### **Résumé of the Changes Produced by Nitrate of Silver.**

**Acute. (Twenty-four hours.)** At the necropsy the mucosa of the lower part of the large intestine was found to be decidedly reddened; there were many transverse rugæ in this part of the intestine. On microscopic examination it is found that the epithelial cells that lined the surface of the gut and those that lay in the mouths and necks of the crypts have entirely shed off. In

the lower portion of the crypts the cells are swollen, irregular in form, and have sometimes desquamated, but the changes are by no means so pronounced as nearer the surface. It is noteworthy that mucin formation seems to have ceased in these cells entirely.

The crypts are somewhat smaller than usual, owing to the accumulation of inflammatory materials in the surrounding tissues.

The interglandular tissues contain a great amount of hemorrhage, and the parts are swollen as a result of the presence of much fluid. A great many polymorphonuclear leucocytes are found in these tissues. These alterations extend to the basal portions of the crypts, but diminish gradually as this part of the mucosa is approached.

The muscularis mucosae is swollen and there are quite a number of polymorphonuclear leucocytes lying between its fibres.

The layer of the submucosa lying next to the muscularis mucosae contains considerable numbers of polymorphonuclear leucocytes, and the bloodvessels in this part of the intestinal wall are considerably dilated.

**Chronic. (Eighteen days.)** At the post-mortem examination the intestine was found to be considerably swollen and its mucous surface was decidedly reddened; here and there over the mucosa there are bright blood-red spots.

On microscopic examination the changes in the intestine are found to vary very much in different situations. For the most part the epithelial coverings of the intestine have suffered no alteration other than that the cells seem to secrete less mucin than is normally the case, and they stain more intensely with basic dyes than usual. Notwithstanding that there are practically no changes in the epithelial lining of the intestine, the interglandular tissues show marked alteration. The lymphatic vessels are distended with fluids, and there have accumulated in the parts enormous numbers of plasma cells. The collagenous tissues stain rather poorly, but the elastin shows no alteration. It is noteworthy that mucin is found in appreciable quantity in the tissues around the basal portions of the glands. The muscularis mucosae is somewhat swollen, and between its fibres there are a few polymorphonuclear leucocytes and lymphoid cells.

In other situations pronounced catarrhal changes are found;

the epithelial cells lining the surface of the intestine and those covering the mouths of the crypts have entirely shed off, but the alterations in the interglandular substance, though perhaps somewhat more intense, are in every way similar to those that occur where the changes on the surface are not so pronounced.

Here and there on the mucous surface there are well-defined ulcers; these extend to varying depths into the substance of the mucosa, sometimes even completely through this layer down to the muscularis mucosæ. When there are remnants of the crypts still in the parts the epithelial cells lining them show surprisingly little catarrhal change; these cells never contain mucin. Between the partially destroyed crypts, and forming the bases of the ulcers, there is much newly-formed fibrous tissue; as might be expected, there are between the fibrils of this tissue great numbers of plasma cells and many lymphoid cells. The surface of these ulcers is not uncommonly covered over by well-developed, newly-formed epithelium.



## CHAPTER V.

### EXPERIMENTS TO DETERMINE THE EFFECTS OF COLCHICUM IN POISONOUS DOSES ON THE LARGE INTESTINES OF DOGS.

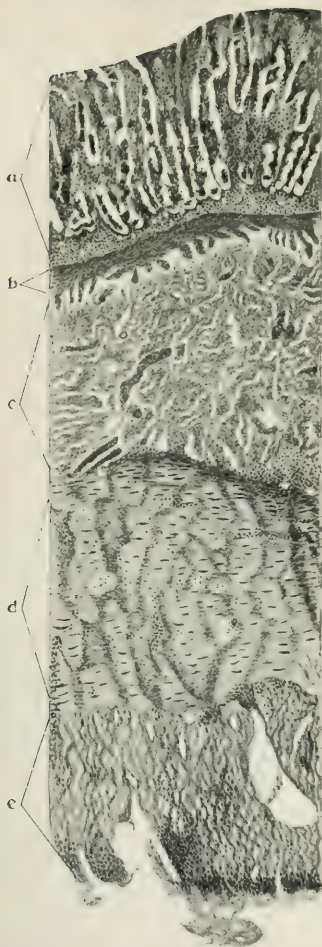
#### EXPERIMENT I. **Duration, probably about twelve hours.**

A DOG weighing about 7 kg. was given 25 c.c. of the fluid extract of colchicum seed at 5.30 P.M., October 18, 1900. At an early hour on the following morning he was found dead.

A post-mortem was at once made, with the following results: The intestinal tract shows but little change, there being only a few hemorrhagic areas on the inner surface of the stomach and several dark bluish-red discolorations on the mucosa of the lower part of the large intestine. These discolorations occur on the tops of the rugæ principally, but the change also extends to the mucosa that lies between them to a certain extent. The affected area shows no swelling. The entire gastro-intestinal tract is empty.

On microscopic examination most exquisite and extensive catarrhal alterations are found in the mucosa of the intestine. Along its free surface there are numerous thick masses of mucin in which there are found many epithelial cells that universally show degenerative changes; there is quite an amount of granular debris also intermixed with this mucin, and many bacteria are present. On close inspection it is found that the surface layer of epithelium is at all points absent, and throughout the crypts most extensive catarrhal changes are apparent. The epithelial cells that lie in the mouths and necks of the crypts are swollen, irregular in form, and, for the most part, have been loosened from their basement membranes; they very generally contain quantities of mucin. In some cases these cells have undergone such extensive changes that masses of partially broken up cells and granular detritus fill the lumina of the glands. Lower down in the bodies of the glands similar alterations also occur, though the





The specimen is from about the middle portion of the large intestine of a dog that had been given by the mouth 25 c.c. of extract of colchicum probably about twelve hours before death occurred. The tissues were fixed in Bensley's solution and stained with carbol toluidin-blue and eosin. Beck  $\frac{1}{2}$  inch, Oc. 1 inch. *a.* Mucosa, showing extensive catarrhal change in the epithelial cells of the surface and of the crypts and swelling of the intervening tissues. *b.* Muscularis mucosae. *c.* Submucosa. *d.* Circular muscular layer. *e.* Longitudinal muscular layer. (Exp. I.)



cells do not show quite the same degree of change that they exhibit near the free ends of the crypts; these cells show, almost without exception, mucin within their protoplasm. It is noteworthy that the tissues intervening between the necks of the glands are swollen to such an extent that the lumina of these structures are often nearly and sometimes entirely closed at the point where they open upon the surface of the intestine.

The elastic tissue that constitutes the basement membranes of the crypts fails to stain in its outer two-thirds, but that upon which the cells in the bodies of the glands rest is entirely unaltered.

Marked degenerative changes have occurred on the surface of the tissues that lie between the crypts; the cells in these situations are very granular, in most cases have lost their nuclei, and all of the contained structures are, as a rule, decidedly acidophilic. Between many of the glands and just beneath the surface there are hemorrhages, which are often extensive, so much so that they completely mask the tissue in which they lie, and, as before remarked, encroach upon the crypts to such a degree that their lumina are completely obliterated. In those areas where no hemorrhages have occurred there is always marked swelling. The cells lying in the swollen tissues usually show evidence of degenerative change, they being quite often decidedly acidophilic, and their nuclei frequently show fragmentation. The blood cells that lie in the hemorrhagic areas likewise show degenerative changes; the hemoglobin is more or less dissolved from the cells, and in quite a number of instances they seem to be in a measure amalgamated together, forming almost homogeneous acidophilic masses. Lower down between the crypts the tissues quite frequently show a slight degree of swelling, but no hemorrhages or marked degenerative changes are to be observed. Throughout the tissues that intervene between the crypts there are numerous, unusually large mucinoblasts. These cells, as a rule, lie just beneath the basement membrane; in some instances they have penetrated through this coat and lie partially or wholly within the lumina of the crypts. These mucinoblasts are breaking up to a marked degree, as free granules that plainly belong to the matured cells are frequently found in the tissues.

The muscularis mucosæ, the submucosa, the muscular coats, and the serous covering of the intestine are entirely normal.

#### EXPERIMENT II. **Duration, probably about fifty-six hours.**

To a dog weighing 8 kg., 12 c.c. of the fluid extract of colchicum seed were given by means of a stomach-tube. On the following day the dog suffered with profuse watery stools, mixed with blood, and the animal was evidently quite weak. After thirty-six hours from the time that the drug was given the dog was much better, and the diarrhoea seemed to have subsided. Six hours later an equal quantity of the fluid extract of colchicum was again administered, and the animal died some time during the ensuing night. Death resulted in from fifty-four to sixty hours after the first dose was given. As soon as the animal was found dead a post-mortem was made and the following observations recorded :

The mucosa of the entire intestinal tract is greatly reddened, the intensity of the process diminishing from above downward. The large intestine is empty and its mucous surface is very red. The apices of the rugæ are distinctly redder than the neighboring mucosa. There is nowhere any appearance of ulceration.

Macroscopic examination of the sections prepared for microscopic examination show no change. On examining the mucosa with a low power most marked alterations are at once apparent. The entire layer of surface epithelium is absent, and in its place a coat of granular debris is found ; the free surface of the layer of granular material is very smooth and uniform and does not exhibit those minute elevations and depressions that are seen on the normal mucosa. This material is almost uniformly acidophilic, there being only here and there cells with nuclei that still take the basic stain feebly. It is largely composed of red blood-corpuscles in varying stages of disintegration ; hæmoglobin has been dissolved out of many of the cells to such an extent that they present the appearance of the so-called "phantom corpuscles" sometimes observed in the urine. Intermingled with these disintegrating red cells there are a few partially broken-up lymphoid cells. There are also quite a number of necrotic epithelial cells, but they are distinguished only by their positions, since they have all lost

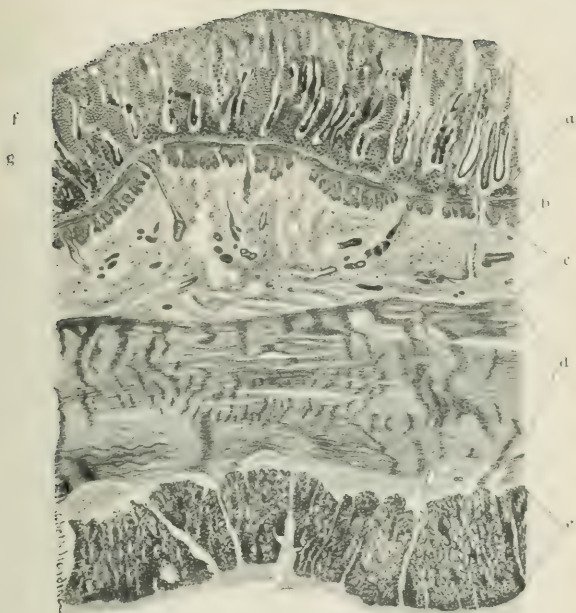
the characteristics of the normal cells. At some points small particles of mucus are found, but the amount of this substance is very small. Throughout this material there are varying numbers of bacteria. Immediately beneath this granular layer, but separated from it by no well-marked line of demarcation, are the tissues of the mucosa. Where in contact with the granular material the tissues are universally acidophilic, and are evidently completely necrotic, but they still preserve enough of their morphologic peculiarities to permit recognition. Passing down into the mucosa the necrotic tissues gradually give way to more or less normal structures. In these situations the epithelial cells of the crypts show everywhere marked degenerative changes, but notwithstanding this present a certain degree of resemblance to the normal cells in their morphologic and staining peculiarities. These cells lie singly or, much more commonly, in clumps. When examined with high powers it is found that they are exceedingly irregular in form, some being spindle-shaped, others oval, and still others rounded; the rounded ones are especially common. In some situations they present a very irregular appearance, which is evidently the result of necrotic changes in and subsequent rupture of the capsules of the cells. The protoplasm of the cells is generally acidophilic, though in many instances the entire cell is so intensely basophilic that it is impossible to make out the nucleus. With high powers the protoplasm of all the cells appear granular, but this is much more marked in the cells the protoplasm of which still exhibits more or less affinity for basic dyes. Many of the cells contain small vacuoles. Small granules of mucin are frequently present within the protoplasm of these cells. A great number of the cells have lost their nuclei, and even in those in which the nuclei are still perceptible they, as a rule, exhibit alterations. The nuclei often lie at the sides of the cells, and either stain very poorly or with unusual intensity. In the former case they preserve their form and usual size and even exhibit poorly stained but still quite distinct particles of chromatin arranged around the inner borders of the nuclear membranes; in these cases the nucleoli are usually very distinct. These cells commonly contain granules that give the mucin reaction. The cells with deeply staining nuclei are not so numerous as those just described, are rounded or oblong in

form, and they are usually crowded together in the centres of the lumina of the crypts. The protoplasm of these cells is more intensely acidophilic and decidedly more homogeneous than that of the cells with the faintly staining nuclei. Within their protoplasm small granules are sometimes present, but not so often as in the other cells. The nuclei are smaller than those of the cells first described, measuring usually about  $3.5\mu$  in diameter. They are unusually rounded, but are often oblong or irregular in form, and sometimes appear to be fragmented. These nuclei stain intensely with all nuclear dyes, and appear almost homogeneous throughout. They contain no nucleoli. In sections stained in some ways there are often seen pale, rounded areas surrounding these masses of chromatin, the nuclear membrane being under these circumstances entirely absent. The foregoing description applies to the necks of the crypts.

Deeper down in the bodies of the glands the condition of the epithelium is in general much the same as nearer the surface. Indeed, it may be said that there is no difference other than one of degree. The epithelial cells are invariably loosened from their basement membranes, but not infrequently remain attached to each other in the same relative positions as in health. Under these circumstances the protoplasm is not quite so basophilic as that of the normal cells, and the nuclei stain somewhat feebly, but the cells are otherwise normal. Internal to this layer of cells, and usually entirely filling the lumina of the crypts, are masses of cells with strongly marked acidophilic protoplasm and deeply staining nuclei, such as have been described in speaking of the changes in the necks of the glands. These cells do not contain mucin granules so often as those that lie in the necks of the crypts, but enough of this substance is present to make it quite conspicuous in properly stained sections. There is also much free mucus among the cells. This mucin formation is of considerable interest, since it is rarely elaborated in the bodies of the glands in health.

The elastic tissue composing the basement membranes upon which the epithelial cells rest is not greatly altered except along the free surface of the intestine, where, as the result of the superficial ulceration, it has entirely disappeared. In the upper portion

PLATE XI.



Specimen from about the middle portion of the large intestine of a dog that had received 12 c.c. of the fluid extract of colchicum about fifty-six hours and a like quantity about twelve hours before death occurred. The tissues were fixed in Bensley's solution and stained with hemalum and eosin. Beck  $\frac{1}{2}$  inch, Oc. 1 inch. *a*. Mucosa, showing necrosis of its free surface, desquamation of the epithelial cells of the lower portions of the crypts (*g*), and hemorrhages into the intervening tissues (*f*). *b*. Muscularis mucosae. *c*. Submucosa. *d*. Circular muscular layer. *e*. Longitudinal muscular layer. Exp. II.





of the crypts it does not stain well, but lower down no alteration is, as a rule, apparent. It is noteworthy that the neighboring fibres of collagenous tissue are better preserved than those composed of elastin.

Between the crypts marked alterations are observed. The tissues are greatly swollen as a result of the increase in the cellular constituents of the parts, collection of fluid in the lymphatics, and enormous dilatation of the bloodvessels. On the free surface of the intestine, and extending downward for a considerable distance, the tissues are in a state of necrosis; the nuclei no longer take the basic stain, but, along with the other structures, exhibit acidophilic affinities. Into this mass of broken-down tissue the dilated bloodvessels extend, and their walls also becoming necrotic and giving way, the blood is poured directly into the diseased areas; as a consequence of this a great many red blood cells are found in these situations. These dilated bloodvessels are most numerous in the convex portions of the rugæ. From the necrotic tissues it is obvious that the blood can easily find its way to the free surface of the intestine, where, as already mentioned, it is present in considerable quantities.

Passing downward toward the muscularis mucosæ the necrotic changes become less and less marked, but do not entirely cease until this coat is reached; around the bases of the crypts the change is very slight. Between the crypts numerous cells are found in the tissues; for the most part these are the larger phagocytes of Metschnikoff (epithelioid cells), but mixed with them are numerous lymphoid cells, a few polymorphonuclear leucocytes, and connective tissue cells. At these points there is also much nuclear disintegration, as is shown by numerous nuclear fragments and much granular, amorphous material. Alterations of a similar kind, but of not quite so marked a character, are found between the bases of the crypts and the muscularis. A very curious feature of the change here is the absence of mucinoblasts; in the normal intestine they are present between the crypts in enormous numbers, but a careful search has failed to reveal the presence of a single one of these cells in the tissues examined.

The muscularis mucosæ is slightly swollen, but no other change

is observed. The elastic tissue network of this layer seems entirely normal.

The submucosa is slightly swollen. There is here also a remarkable decrease in the number of mucinoblasts, there being scarcely any of them remaining in the tissues. Immediately beneath the muscularis there are considerable collections of lymphoid cells and a few polymorphonuclear leucocytes in the tissues of the submucosa, these usually lying around the smaller bloodvessels. In these situations there is often considerable cellular fragmentation, the connective tissue cells seeming especially to suffer. The collagenous tissue of the submucosa has not apparently undergone any alteration, but the elastin does not universally stain in a perfectly normal manner; the external elastic lamina of the smaller arteries have suffered most. The epithelial cells lining the inner coats of the bloodvessels are swollen. Where lymph nodes are present some of their cells always exhibit fragmentation, and there are numerous large phagocytes in the lymph channels in and around them.

The circular muscular coat is markedly swollen; for the most part the individual fibres can be seen to be much further separated than they are in health, but scattered throughout this layer there are irregularly shaped collections of fibres that preserve their normal relation to each other. Especially under low powers the appearances that result from this condition in transverse sections are very striking. The elastic tissue network between the fibres is little if any altered.

The longitudinal muscular coat presents the same alterations that are shown in the circular layer, but differ in that they are never so marked.

The subserous and serous coats are normal.

### EXPERIMENT III. Duration, about six and a half days.

Subacute changes in the large intestine resulting from the administration of colchicum.

To a dog weighing 7 kg., 4 c.c. of the fluid extract of colchicum were given by the stomach every two days until the animal had received four doses; it died during the night following the last

dose. After the administration of the drug diarrhoea set in, the dog presented unmistakable evidence of being quite sick, and after each succeeding dose grew worse until death resulted. No blood was ever observed in the stools of the animal, but there was much mucus.

On post-mortem examination the large intestine was found to be contracted, very pale externally, and almost entirely empty. The mucosa showed but little change in the upper portion of the gut, but lower down was distinctly reddened; the change, as usual, was found most pronounced on the tops of the rugae. The small intestine showed similar alterations, but the condition was by no means so marked as in the large gut.

Sections prepared for microscopic examination show no change to the unaided eye. On microscopic examination it is found that the surface epithelium has been entirely eroded away, and, in some situations, its place is occupied by a thin layer of mucus and necrotic material. The epithelium of the entire crypts shows more or less catarrhal change. This, as might be expected, is most marked in the upper two-thirds of these glands, where the changes are universally quite severe. In these situations the cells are frequently detached from their basement membranes and lie singly or in clusters in the lumina of the crypts; they are rounded, oval, or irregular in form, their protoplasm is intensely acidophilic, and quite frequently the nuclei no longer stain with basic dyes. In some instances the nuclei show marked alterations, but in others they appear smaller than normal, are surrounded by no nuclear membrane, and are intensely basophilic; this last characteristic is, when present at all, so pronounced that the nuclei appear perfectly homogeneous throughout. In some cases the cellular membrane has ruptured, and the cells are evidently in varying stages of disintegration. When stained properly these cells invariably give more or less pronounced mucin reaction, and mucin is found between them. Not infrequently there are present toward the free ends of the crypts small, oval-shaped, cystic dilatations varying very much in size, some being but little larger than the crypts and others having diameters two or three times as great. In the centres of these crypts there are collections of cells with deeply staining nuclei and intensely acido-

philic protoplasm that exhibits the mucin reaction. These cells in every way resemble those already referred to as being frequently present in the undilated crypts. Between these cells more or less free mucus is invariably found. Surrounding these masses of cells there is always a distinct layer of nearly normal epithelium, but this is usually detached from the basement membrane. The cells found in these cysts in every way resemble those that occur in the crypts in the more acute changes resulting from colchicum.

In the deeper portions of the glands the epithelial cells very generally remain attached to their basement membranes, but the vast majority of them exhibit the mucin reaction. Quite a number of these cells have, however, degenerated, and, under these circumstances, they exhibit the usual change—*i. e.*, the cells are extremely irregular in form, their protoplasm is unusually acidophilic, and their nuclei stain feebly or not at all with basic dyes. Occasionally there are also seen rounded or oval cells, with intensely acidophilic protoplasm and small, deeply staining nuclei; here, as elsewhere, these cells always lie loosely in the lumina of the crypts.

In the upper portion of the crypts, where the catarrhal changes are most marked, the elastic basement membranes do not take the stain well, evidently being in a degenerate condition.

The supporting structures that lie between the crypts show but little change except at the free surface of the gut, where, as has been before stated, the desquamation of the epithelium has left them entirely exposed where not covered by mucus. The tissues are somewhat swollen as the result of the dilatation of the lymph vessels, and always show a mild degree of degenerative change. There are present here many large phagocytes, quite a number of connective tissue cells, and a few lymphoid cells. Along the free surface of the intestine the protoplasm of these cells is abnormally acidophilic, and the nuclei are often fragmented and do not stain well. The collagenous tissues of the same regions are granular and are universally acidophilic, but are much less altered than the neighboring elastic tissues. The tissues here frequently contain small bacilli that appear to belong to the colon group. The bloodvessels are contracted and contain but little blood. All

through the upper portion of the mucosa there is the same remarkable absence of mucinoblasts observed in the previous case. The tissues between the bases of the crypts show no change, with the exception that the mucinoblasts have almost entirely disappeared, and the few that still remain are small, ill-formed, and do not give the mucin reaction distinctly. The fibres of the muscularis mucosæ are pushed apart by fluids that have collected in the parts, but further than this there are no changes.

The submucosa is slightly swollen, but is otherwise normal.

The circular muscular coat is somewhat swollen. The elastic network shows no change.

The longitudinal muscular coat is also somewhat swollen, but no other change is found.

The subserous and serous coats are normal.

### **Résumé of the Changes that are Produced in the Intestine as the Result of the Administration of Colchicum.**

**Acute. (Twelve hours.)** The mucous surface of the intestine shows here and there dark bluish-red discolorations, occurring principally on the tops of the rugæ. The intestine otherwise appears normal.

The epithelium that lined the surface of the intestine in health is for the most part absent, and that that covered the mouths and necks of the crypts has in many instances shed off. The cells of the deeper portions of the crypts present slight catarrhal change, and all contain more or less mucin. The glands are considerably compressed toward their free ends, which is the result of the collection of fluids and cells in the intervening tissues.

The interglandular tissues contain numerous hemorrhagic areas. The pre-existing cells, as well as the red blood cells that have been poured into the parts, generally show necrotic changes. Mucinoblasts are very numerous and quite large; they are sometimes found in the lumina of the crypts.

**Changes less acute than the preceding. (Fifty-six hours.)** At the post-mortem the large intestine of the animal was found empty and the mucous surface of the gut was very red.

On microscopic examination the surface layer of epithelial cells

was found entirely absent. The cells have likewise shed off from the mouths and necks of the crypts, and frequently lie in the openings of the glands in varying stages of disintegration. In the bodies and bases of the crypts the cells are swollen and irregular in form, and have not uncommonly desquamated; but in these situations, even when not attached to their basement membranes, they generally stain in practically a normal way. All of the epithelial cells found, even the necrotic cells at the mouths of the crypts, show within their protoplasm more than the usual quantity of mucin.

The interglandular substance is necrotic on its free surface, and the tissues are decidedly swollen somewhat lower down. In the latter situations the bloodvessels are universally enormously dilated and have in many instances ruptured, with the result that quantities of blood are found everywhere in the tissues. There are no changes in the normal cellular constituents of the parts further than that mucinoblasts are entirely absent. There are here and there small collections of polymorphonuclear leucocytes.

The submucosa is slightly swollen, and there are found in the lymph spaces here and there a few polymorphonuclear leucocytes.

**Subacute. (Six and a half days.)** On examination the intestine was found empty and its mucous surface generally pale, though over the lower half of the large bowel the mucosa was somewhat redder than that of the upper portion of the gut.

On microscopic examination the surface layer of epithelium is found to have entirely disappeared, and the cells that lined the mouths and necks of the crypts have likewise desquamated. The epithelial cells in the bodies and bases of the crypts are swollen and irregular in form, and in some instances have shed off from their basement membranes. Almost all of the cells contain mucin, so that this substance is evidently being formed in more than the usual quantity.

The free surface of the interglandular tissues are distinctly necrotic. At a short distance below the surface the tissues lying between the crypts are somewhat swollen as a result of the presence of increased quantities of fluids in the parts. The bloodvessels, instead of being dilated, generally appear to be somewhat contracted. Mucinoblasts are almost entirely absent.

## CHAPTER VI.

### EXPERIMENTS TO DETERMINE THE EFFECTS PRODUCED BY PURE CARBOLIC ACID ON THE LARGE INTESTINES OF DOGS.

#### EXPERIMENT I. **Duration, between twelve and twenty-four hours.**

ON February 6, 1901, at 11 A.M., 10 c.c. of pure carbolic acid were injected into the large intestine of a medium-sized dog. On the following morning the animal was found dead, and an autopsy was at once made.

On examination the lower half of the intestine was found to contain a small quantity of fecal matter. The walls of the gut in this situation were thickened, and they were so stiff that it required some little force to push them together before the viscus was cut open. The mucosa was of a grayish-red color and presented the appearance of superficial ulceration. The rugæ were not numerous, nor were they very prominent; the mucosa covering them presented an appearance in every way similar to that of the neighboring portions of the gut.

On microscopic examination it was found that the epithelium that covered the surface of the intestine and the tissues that lay immediately beneath have entirely disappeared, there being in their stead a mass of granular material containing much mucus. The epithelial cells lining the mouths of the crypts have likewise in some instances disintegrated and disappeared, but the tissues intervening between these portions of the glands, though greatly degenerate, are still present in their normal situations. The cells lining the necks of the crypts are generally still attached to their basement membranes, and, without exception, their protoplasm is almost entirely made up of mucin. Those parts of the protoplasm of the cells that do not consist of mucin are finely granular and take basic stains in preference to acid ones; as the nuclei

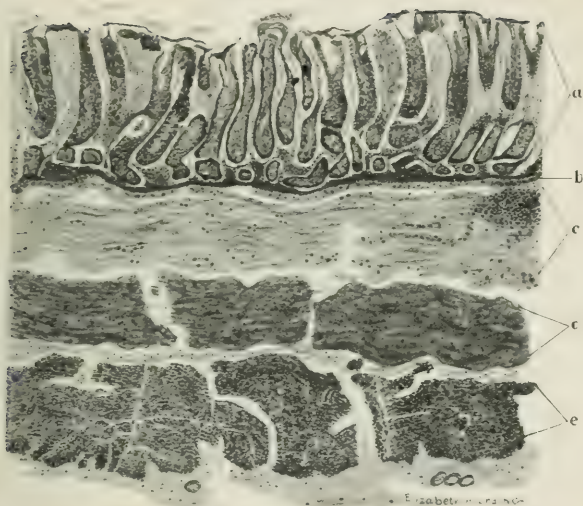


are visible in none of the cells, this in all probability is the result of the fact that they have disintegrated and the nuclear substance has been diffused into the surrounding protoplasm. The cells lining the bodies of the glands show no alteration further than that their protoplasm is made up almost entirely of mucin. The epithelial cells lying in the basal portions of the glands appear much shorter than normal, and the protoplasm toward the free ends of the cells is invariably filled with mucin. In every instance the crypts are completely filled with masses of mucus, this substance being very largely present even in the basal portion of the lumina of the crypts. In the deeper portions of the glands the protoplasm of the epithelial cells seem to have undergone a mucin transformation, and in most instances the cells have ruptured—which would account for the fact that the cells appear much shorter in the situations referred to than they are found in health. In the regions most diseased the basement membranes of the crypts no longer take their specific stains and cannot be made out with certainty.

As has already been remarked, the superficial portions of the interglandular substance projects into the lumen of the gut, the epithelial cells normally covering these structures having entirely sloughed away. Of those that are normally present the only structures that still remain in this area are the bands of collagenous tissue, between which there is present a granular debris that has resulted from the destruction of the pre-existing cells and of the red blood-corpuscles that have emigrated into the part. The tissues here, as a rule, are slightly basophilic; this appears to have been the result of the disintegration of the pre-existing cells of the part and the diffusion of the chromatin that was contained within them into the surrounding tissues. Deeper down between the necks and bodies of the glands the tissues are considerably swollen, this being due to the rupture of the blood-vessels and to the effusion of blood into the surrounding tissues. The red blood cells composing these ecchymotic areas have universally undergone degenerative change, and there remains nothing except a granular debris representing them. As a result of this the tissues stain in an almost uniform manner with acid dyes, the granular debris resulting from the disintegration of the red



PLATE XII.



Specimen from about the middle portion of the large intestine of a dog into which 10 c.c. of pure carbolic acid had been injected from twelve to twenty-four hours before the death of the animal. The tissues were fixed in Bensley's solution and stained with haemalum, muchematein, and picric acid. Beck  $\frac{1}{2}$  inch. Oc. 1 inch. *a*. Mucosa, showing all of the crypts filled with mucin, and the intervening substance swollen and more or less necrotic. *b*. Muscularis mucosae, the tissues of which stain very badly. *c*. Submucosa, the tissues of which also refuse to take the stain in the usual way. *d*. Circular muscular layer. *e*. Longitudinal muscular layer. (Exp. I.)



blood cells and the collagenous tissue being colored almost exactly alike. In specimens prepared by Van Gieson's method the structures found in these situations are dyed a reddish-yellow hue, the bands of collagenous tissue being no longer colored of the intense red color which they assume under normal conditions when stained in this way. In the interstices of the tissues there are quite a number of lymphoid cells, pseudoplasma cells, and a few polymorphonuclear leucocytes, none of which stain in a perfectly normal way; the chromatin in the nuclei of these cells seems to have been diffused through their protoplasm, with the result that the entire cells show in all of their parts more or less affinity for basic dyes, and the nuclei are never brought out in a precise or clear manner. Mucinoblasts are absent not only from the interglandular substance here, but are nowhere found within the mucosa. Passing down toward the bases of the glands the changes in the tissues gradually become less marked, there is not so much blood effused into the parts, the cells stain more distinctly, and it is not uncommon to find bloodvessels the walls of which are still preserved, though they are enormously dilated and contain thrombi composed of white blood-corpuscles and disintegrating red blood cells. Of course, as a result of the swelling which has occurred between the crypts these structures are more or less compressed; but this is not so markedly the case as one might suppose, for they, as a rule, do not measure less than  $60\mu$  in diameter. Changes of a similar kind are likewise found around the basal portions of the glands, but they are not altogether so intense, there being but little blood in the tissues here, and the cells that are present stain fairly well.

The muscle fibres composing the muscularis mucosæ have in a large measure disintegrated, which doubtless explains the fact that but few rugæ were found on the surface of the intestine at the time that the post-mortem was made. In many cases the forms of the muscle fibres are in a measure preserved, but in all instances in the regions that have suffered most change they consist of a mass of acidophilic granules, and their nuclei take the basic stain but slightly or not at all. Quite as commonly the cells have entirely broken up and are represented by a mass of granular debris lying loosely in the tissues. The elastic tissue network

of this layer has likewise disintegrated and no longer takes its specific stains.

The tissues composing that layer of the submucosa that is in contact with the muscularis mucosae are in a partially degenerate condition. The elastic tissue fibrils can no longer be detected, and the collagenous tissue bands are swollen, and when stained by the method of Van Gieson are, like the tissues lying between the crypts, colored reddish-yellow instead of the bright red hue which they assume under normal conditions when treated in this way. The nuclei of the connective tissue cells in this area do not stain with their usual intensity with basic dyes. No mucinoblasts are found in the deeper layers in any of the parts of the diseased tissues. In the deeper portions of the submucosa the elastic tissue and collagenous tissue fibrils stain in a normal way, and there appears to be practically no change in the tissues. The blood-vessels in all parts of the submucosa are enormously distended and contain thrombi in which are found white blood cells and many disintegrating red blood-corpuscles; no fibrin is ever found in these vessels. The walls of the vessels in the superficial portions of the submucosa stain as do the surrounding tissues, and have evidently undergone decided degenerative change. In the deeper portions of the submucosa the walls of the vessels are intact with the exception only that the epithelial cells lining them have shed off, exposing the elastic tissue basement membranes beneath, which always stain in a normal manner.

No changes are found in the other coats of the intestine, with the exception that the walls of the bloodvessels show slight alteration; the lining epithelial cells have usually shed off from their basement membranes, and may even be found lying loosely in the lumina of the vessels.

#### EXPERIMENT II. **Pure carbolic acid. Duration, eighteen days.**

On February 6, 1901, 2 c.c. of pure carbolic acid were injected into the rectum of a large dog. The animal appeared to suffer no ill effects as the result of the administration of the drug. Injections of a like quantity of the acid were given on the 8th, 10th,

12th, 14th, 16th, 18th, 20th, and 22d of February. The dog grew somewhat thinner during the course of the treatment, and after the acid had been given several times he suffered with diarrhoea; the stools contained much mucus mixed with blood. On February 24, 1901, the animal was killed with chloroform, and an autopsy was at once made. The large intestine was found to be practically empty, the mucous surface of the lower half of the gut was of a reddish-gray color, with here and there areas that were intensely blood-stained. The mucosa presented the appearance of superficial ulceration. The rugae were not particularly numerous in the area showing the greatest amount of alteration, but somewhat higher up these elevations were very prominent both as regards number and size; the mucous membrane covering their apices did not appear more greatly affected than that of the surrounding portions of the intestine. The gut was decidedly swollen in the affected regions.

On microscopic examination varying degrees of alteration in the mucosa were found, evidently depending upon whether the parts had been with greater or less frequency subjected to the action of the acid. In some areas the only changes observed are a desquamation of the epithelial cells that normally covered the surface of the intestine and slight catarrhal changes of the epithelial lining of the mouths and necks of the crypts. Under such circumstances there are generally found very large plugs of mucin in the mouths of the crypts that in every way resemble those found in the more acute process, except only that they are not, as a rule, so large. The cells lying in the deeper portions of the glands show no alterations further than that they generally contain more mucin than is usual in health. These masses of mucin seem to have plugged up the openings of the crypts in some instances, and the collection of secretion beneath has caused a mild degree of dilatation of the bodies and bases of the glands; the contents of the resulting cysts consist of a small amount of mucin, intermingled with which there is much granular debris. The cells lining these cystic dilatations of the glands show but little alteration, the only change observed is that they have the appearance of being somewhat swollen. While the deeper portions of the crypts are, as a rule, not affected, some of them present striking

catarrhal changes, this having gone on to such an extent in a few instances that the glands have been entirely stripped of their epithelium. It is of interest to note that the protoplasm of the epithelial cells in and around the diseased areas contain a great many minute granules that take the basic stain; these granules are often present in such numbers that the cells appear of an almost uniform dark color after staining in toluidin-blue and eosin. The basement membranes lying beneath the catarrhal epithelium, as a rule, fail to take their specific stains, but around the basal portions of the glands there is no obvious alteration in these structures.

The interglandular substance in these situations is decidedly swollen as a result of the presence of quantities of fluids in the parts. Generally there is a notable absence of the cellular constituents that are usually found in these situations, the cells appearing to have been carried away by the lymph currents. This change, as a rule, is only confined to the supporting structures lying between the mouths and necks of the crypts, but in some instances almost all of the cells that originally lay between the glands have disappeared. Of the cells that still remain in the parts a very large percentage consists of mucinoblasts, which have evidently increased considerably in the affected region. The collagenous and elastic tissue fibrils show no change.

The tissues lying deeper down beneath the lesions that have just been described show no alterations.

In some situations the changes are of a more pronounced character. Here there has been quite a degree of ulceration of the mucosa, the process extending to a variable depth into the tissues. The surfaces of these ulcerated areas are composed of a granular debris resulting from the destruction of the pre-existing tissues of the parts, and along with this there are quite a number of polymorphonuclear leucocytes and a few lymphoid cells. There is no clear line of demarcation between the partially necrotic tissues of the surface and the normal ones that lie at a lower level, as they merge insensibly into each other. The epithelial cells that line the remnants of the glands show no very pronounced alteration further than that their protoplasm is somewhat more basophilic than is usual; exceptionally, they exhibit catarrhal

changes, and in some instances have entirely shed off from their basement membranes. The intervening supporting tissues are swollen as a result of the accumulation of fluids and the dilatation of the bloodvessels, and of the accumulation in the parts of polymorphonuclear leucocytes, lymphoid cells, plasma cells, and quite a number of the large phagocytes of Metschnikoff.

The tissues lying beneath these lesions show alterations depending upon the depth to which the ulceration extends; when the changes are superficial the alterations, as a rule, do not extend below the mucosa; but in instances where they pass downward more deeply the muscularis mucosæ is in some cases swollen, and there are sometimes found between the muscle fibres small collections of polymorphonuclear leucocytes; where the necrotic processes are quite extensive the upper layer of the submucosa may show alterations of a similar kind.

In some cases the entire mucosa has been destroyed, though the actual ulceration was never observed to extend below the muscularis mucosæ. The floors of such ulcers are composed of a granular débris, intermingled with which there are many polymorphonuclear leucocytes and lymphoid cells. In the neighboring partially normal tissues there are numerous polymorphonuclear leucocytes, a great many gigantic mucinoblasts, multitudes of large phagocytes of Metschnikoff, and a few lymphoid and plasma cells; the connective tissue cells that originally lay in the parts have for the most part disappeared. These changes extend downward through the muscularis mucosæ into the outer layers of the submucosa, but, becoming gradually less marked, finally cease altogether in the vicinity of the circular muscular coat. Fibrin is never found in the diseased areas, nor does there appear to have been an increase in the collagenous tissues. On the surfaces of the ulcers both the collagenous and elastic tissue fibrils fail to take the stain in a normal way, but lower down they present no alteration. It is noteworthy that the newly-formed epithelium has partially grown over the surfaces of the ulcerated areas in many instances; these recently formed epithelial cells are large and quite tall near the points where they come in contact with the epithelium of the surrounding normal tissues, but as they grow away over the diseased surface they become smaller and



smaller, and finally terminate in minute, flattened cells at a greater or less distance from the edges of the ulcers. These cells often contain mucin, and mitoses are sometimes observed within them.

From the preceding description it will be seen that there result in the tissues, from the repeated application of carbolic acid, changes closely simulating those that are found in the bowel in the subacute forms of amœbic dysentery.

No changes are observed in the other coats of the intestine.

### **Résumé of the Changes Produced by Carbolic Acid.**

**Acute. (Twenty-four hours.)** At the necropsy the gut was found to be decidedly thickened and much stiffer than usual. The mucosa presented the appearance of superficial ulceration.

On microscopic examination it is found that the superficial epithelium and that lining the mouths of the crypts has entirely disappeared. The epithelial cells lying in the lower portions of the glands still line their basement membranes in the normal way ; but they have within them, without exception, great masses of mucin. The lumina of the crypts are in all instances likewise completely filled with this substance.

The interglandular tissues contain great quantities of blood, the cells of which have entirely disintegrated. The granular debris that results from the breaking up of the red blood cells is present in such quantities that none of the pre-existing tissues of the parts can be made out.

The muscle fibres of the elastic tissues constituting the muscularis mucosæ show pronounced degenerative change.

The connective tissues of the submucosa do not stain well, and they are evidently in a more or less degenerate state. The blood-vessels in this coat are greatly dilated and are not uncommonly thrombosed. The walls of these vessels likewise show degenerative change. No mucinoblasts are found in any part of the intestinal wall.

**Chronic. (Eighteen days.)** On post-mortem examination the walls of the lower portions of the large intestine were found decidedly swollen, and the mucosa was somewhat redder than usual.



Microscopic examination shows that the changes in the intestine vary very much in different situations. In some cases there are only slight catarrhal alterations, but it is noteworthy that there is a greatly increased amount of mucin being formed in all instances. The epithelial cells, even where otherwise normal, appear unusually basophilic. The basement membranes upon which these cells lie do not stain well.

The interglandular tissues here are decidedly swollen as the result of the presence of fluids. The tissues contain an unusual number of mucinoblasts.

In some cases there is actual ulceration of the mucosa, which extends to a much greater depth in some situations than in others. In these areas the epithelial cells lining the remnants of the crypts show comparatively little change, but the intervening tissues are generally swollen and contain, in addition to fluids, many polymorphonuclear leucocytes, lymphoid cells, plasma cells, and large phagocytes of Metschnikoff. The bloodvessels here are decidedly dilated.

In some instances the ulceration extends down into the muscularis mucosæ, the fibres of which are decidedly granular and are frequently pushed apart by collections of polymorphonuclear leucocytes. Where the ulcers are old newly-formed epithelium has grown out over them from the surrounding epithelial surface in many instances.

## CHAPTER VII.

### EXPERIMENTS TO DETERMINE THE EFFECTS OF SOLUTIONS OF COPPER SULPHATE ON THE LARGE INTESTINES OF DOGS.

#### EXPERIMENT I. **Duration, forty-eight hours.**

To a dog weighing 8 kg., 4 gm. of copper sulphate dissolved in 50 c.c. of water were given by the mouth. The dog had been previously anesthetized, so that the drug was not vomited. Twenty-four hours later the animal frequently vomited, and was evidently quite sick. On the following day—forty-eight hours after the first dose was given—4 gm. of copper sulphate were again administered in 50 c.c. of water. Notwithstanding that a part of this was vomited, the animal shortly after passed into a state of collapse and died in an hour from the time the chemical was given.

A post-mortem was at once made. The large intestine was found practically empty. Its mucosa was moderately reddened, the tops of the rugae showing, as usual, the greatest degree of change. The small intestine exhibited a similar alteration, but to a much less degree.

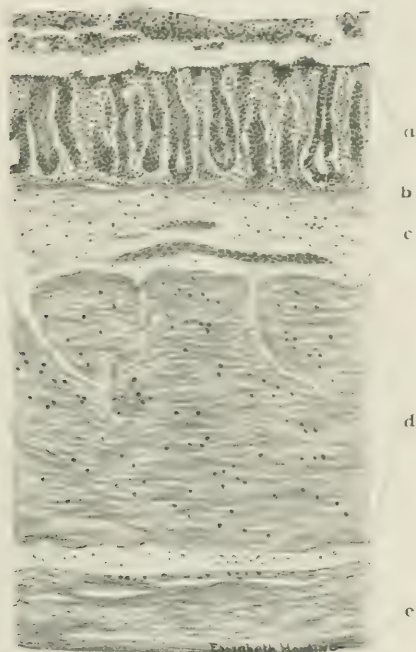
Microscopic sections when viewed with the unaided eye show no alteration.

On microscopic examination the superficial epithelial layer is found very generally absent, and, taking its place, there is an almost uniform, very thin layer composed largely of mucus, intermingled with which there are numerous bacteria and some granular debris. Further than that there are a greater number of mucin-bearing cells than normal, the epithelial cells of the crypts show no change except immediately at their mouths, where, occasionally, a few of the cells have desquamated. There are about the usual number of mitotic figures in the basal cells.

The elastic tissue basement membrane is not greatly changed,

PLATE XIII.

f



Specimen from about the middle portion of the large intestine of a dog that had received by the mouth a solution of copper sulphate forty-eight hours, twenty-four hours, and again one hour before death occurred. The tissues were fixed in Bensley's solution and stained with haemalum, muchæmatein, and picric acid. Beck  $\frac{1}{4}$  inch, Oc. 1 inch. *a.* Mucosa, upon the surface of which there is a mass of mucus containing a granular debris (*f*), and between the crypts there are found multitudes of free red cells, many large phagocytes and a few polymorphonuclear leucocytes. *b.* Muscularis mucosæ. *c.* Submucosa. *d.* Circular muscular layer. *e.* Longitudinal muscular layer. (Exp. I.)



but takes the stain badly or not at all from the middle of the crypts outward to their ends.

The tissue that intervenes between the crypts is about as often normal as otherwise, but in some situations, especially at the apices of the rugæ, shows marked alteration; while there appears no plausible explanation for this peculiarity of the lesions produced by copper sulphate, the change is so pronounced and of such a peculiar kind that it appears to be entirely characteristic. In the affected regions the crypts are widely separated by disintegrated blood, and, in addition to the blood cells, there are found many lymphoid cells, quite a number of pseudoplasma cells, and a comparatively large number of phagocytes. The phagocytes contain in some instances nucleated cells, but always many necrotic red cells. The collagenous tissue, even in the areas most affected, is practically normal; however, in some instances it takes the stain poorly. No bloodvessels can be made out in the diseased region. The changes are limited almost entirely to the outer half of the mucosa, but sometimes extend even to the muscularis mucosæ.

In the otherwise healthy regions the bloodvessels sometimes rupture, and there of course results a localized area of hemorrhage around the affected vessel. In instances where this change has existed for quite a time the cells found in and around the diseased area exhibit similar alterations to those observed in the more pronounced lesions just described. At no point in the mucosa are there dilated bloodvessels; indeed, the vessels, if their calibre be at all changed, seem smaller and less conspicuous than normal.

The mucinoblasts have entirely disappeared from the deeper portions of the mucosa, but a few are still present in the superficial regions; these cells are, however, smaller than normal, and at most contain only a few small mucin granules clinging to their nuclei.

The muscularis mucosæ is entirely normal.

The submucosa is normal, with the exception that the mucinoblasts are diminished in number and are smaller than the cells of a like kind found in the normal intestine.

The muscular coats are normal.

The subserous and serous coats show no change.

**EXPERIMENT II. Duration, about seventy-five hours.**

On May 27, 1900, at 9 P.M., 4 gm. of copper sulphate dissolved in 50 c.c. of water were injected into the rectum of a dog weighing 6.5 kg.; before the drug was given the animal was thoroughly narcotized. On removing the rectal tube a small quantity of the copper sulphate solution ran out.

On the following morning the dog could not be induced to get up, and exhibited every evidence of being very sick. On May 30th, at 8 P.M., the injection was repeated. The animal died during the night. The post-mortem was made early the following morning.

The large intestine contained a considerable quantity of a dark brick-red grumous substance that appeared to consist largely of disintegrated blood. The surface of the intestine is of precisely the same color as the material contained within it. On close inspection the more elevated portions are found to be somewhat darker in color than the intervening depressions.

On microscopic examination of sections of the diseased intestine the mucosa is found to be entirely destroyed, but here and there are necrotic masses which, from their situation, are evidently remains of the structures contained in this layer.

The muscularis mucosae has also, in most instances, entirely sloughed away, and even where fragments of it remain the tissues are in a state of advanced disintegration; it is noteworthy that the elastic tissue network of this coat is still demonstrable by the method of Weigert. These various necrotic structures take the place of the mucosa and form a sort of lining for the intestine. The submucosa is greatly swollen, partly as the result of accumulations of liquids in the lymph spaces and, to an even greater extent, of an enormous collection of cells in the same situations. These cells are present in greater number in the outer layers of the submucosa, just beneath the sloughing tissues of the outer coats. In these situations many bacteria are present, and, it may be added, that they are also numerous in the deeper portions of the necrotic tissues. These bacteria are present in such numbers that it seems highly probable that they are responsible for a part, at least, of the changes that are present. The cellular masses that

make up the great bulk of the tissues in the outer layer of the submucosa are made up of a great number of lymphoid cells, many red cells, and a few transitional and polymorphonuclear leucocytes; the leucocytes are apparently not present in greater number than would be warranted by the hemorrhage that has evidently occurred in the parts, and the process cannot therefore be regarded as being in any sense a suppurative one. In this part of the submucosa the fibrils of collagenous tissue, further than being widely separated from each other, show no change; but the elastic tissue stains badly in many situations, and appears to have suffered more than the neighboring fibrous structures. The bloodvessels are here always thrombosed and contain masses of disintegrating blood. The walls of the vessels show marked alterations; in most all instances the epithelial cells have desquamated, the internal and external lumina stain feebly, and the muscle fibres are swollen and granular, and their nuclei take basic dyes badly.

Passing deeper into the submucosa these cells rapidly decrease in number, the collagenous fibres are not as widely separated from each other, the elastic tissue stains somewhat better, and such marked changes on the walls of the bloodvessels are no longer observed. However, the bloodvessels are not entirely normal, for they are dilated with blood, and degenerative changes in their walls may be still seen here and there; those changes are evidently in many instances sufficiently great to permit rupture of the vessel, since the lymph spaces contain considerable quantities of blood in many localities. These localized areas of rhexis in every way—barring situation—resemble those that have been described as occurring in the mucosa in the milder degenerative process produced by copper sulphate. The submucosa mucinoblasts have entirely disappeared.

The muscular fibres of the circular coat are almost universally considerably separated from each other by accumulations between them of albuminous fluids and a few lymphoid cells. The fibres themselves in some instances appear faintly granular, but for the most part show no alteration. The elastic tissue network of the layer stains poorly, but the collagenous tissues appear to be normal. The bloodvessels show no change.

The longitudinal muscular coat shows a similar swelling be-

tween the fibres, but not to such a degree as was found in the circular layer, and the elastic tissue stains poorly. No further alteration is present.

The bloodvessels of the subserous coat are generally dilated and filled with blood, but their walls show no change further than that the elastic layers stain badly.

The elastic basement membranes of the serous coat stain poorly, but there is no other change observed in this layer.

Not a single mucinoblast was found in any part of the intestinal walls that were examined.

### **Résumé of the Changes Resulting from the Administration of Copper Sulphate.**

**Acute changes following the administration of the drug by the mouth. (Forty-eight hours.)** On post-mortem examination the large intestine of the dog was found empty, and its mucous surface was moderately reddened.

Microscopic examination showed that the surface epithelial cells have entirely shed off, and that the cells lining the mouths of the crypts have likewise desquamated. The cells covering the necks, bodies, and bases of the crypts show no further alteration than that mucin is present in unusual quantities within their protoplasm.

The crypts, as a rule, are compressed and widely separated from each other as a result of the accumulation in the interglandular tissues of great quantities of blood, intermingled with which there are the usual cells found in the parts and many large phagocytes: a few polymorphonuclear leucocytes are also found. There are still a few mucinoblasts present in this area; they are small and contain only a few mucin granules. These changes are almost entirely confined to the outer half of the mucosa. It is a rather curious fact that in the deeper portions of this coat no mucinoblasts are found.

**Acute changes following rectal injection of solution of copper sulphate. (Seventy-five hours.)** On post-mortem examination the large gut was found to contain a considerable quantity of dark brick-red, grumous material resembling disintegrated



blood. The surface of the intestine is practically of the same color as the peculiar substance just referred to.

The mucosa is almost entirely destroyed, there being only here and there small masses of necrotic tissue in which it is possible to recognize some of the structures that go to make up the surface layer of the intestine. In most instances the muscularis mucosæ is also destroyed.

The submucosa, especially that part of it just below the muscularis mucosæ, is greatly swollen as a result of the accumulation of fluids in the parts and of an enormous amount of hemorrhage; there are quite a number of lymphoid cells scattered through the tissues as well as a few polymorphonuclear leucocytes. The bloodvessels are, without exception, thrombosed within this area, and contain masses of disintegrated blood. The epithelial cells that line the bloodvessels have generally shed off from their basement membranes, and the walls in addition to this have evidently suffered considerably, as they present decided evidences of necrotic change. Alterations similar to these are found in every part of the submucosa, but in the deeper portions they are by no means so marked.

The muscle fibres of both the muscular coats are more or less separated from each other by the accumulation of fluids, and there are here and there found a few lymphoid cells. The muscle fibres themselves present practically no alteration.

The subserous and serous coats show no marked changes.

It is a remarkable fact that mucinoblasts are entirely absent from all parts of the intestinal wall, not a single one having been found in any of the numerous sections examined.

## CHAPTER VIII.

### EXPERIMENTS TO DETERMINE THE EFFECTS OF REPEATED DOSES OF CALOMEL GIVEN BY THE MOUTH ON THE LARGE INTESTINES OF DOGS.

#### EXPERIMENT I. **Duration, about four and a half days.**

ON November 13, 1900, a dog weighing 7 kg. was given 0.5 gm. of mercurous chloride by the stomach, and on the following day the dose was repeated. The animal suffered with diarrhœa, and was evidently very sick for two days following. On November 17th a like amount of the drug was again administered. The dog was found dead on the following morning.

At the necropsy the entire intestinal tract was found to contain a soft, grumous material that seemed to be disorganized blood. On examination the mucosa of the large intestine showed but little alteration, there being only here and there minute reddened areas over its surface that are usually, as in almost all of these experimental inflammations, most marked on the tops of the rugæ. The lower part of the large intestine has suffered somewhat more than the upper portion. The edges of the ileocecal valve are decidedly reddened, this, however, being most marked on the upper side. The mucosa of the small intestine is decidedly reddened.

On microscopic examination the surface of the large intestine is found almost entirely free from mucus, but in some situations small masses of granular débris mixed with mucin are present. The surface epithelium has universally desquamated, and the epithelial cells lining the mouths and necks of the crypts have also separated from their basement membranes.

Quite often the cells in the mouths of the crypts, after having been loosened from their basement membranes, have been discharged into the intestinal tract and carried away, but in the majority of instances they still remain in the lumina of the

crypts, clumped together in small, irregularly shaped masses. The cells in the necks of the crypts are, as a rule, still attached to their basement membranes, but in a certain proportion of cases they lie loosely in the lumina of the glands, and in some instances form clumps such as have been described as occurring in the mouths of the crypts. These loose cells are swollen, granular, and quite irregular in form; but their nuclei always stain practically in a normal manner, and their protoplasm, instead of exhibiting the usual acidophilic affinities of degenerating cells, often shows a decided tendency to take the basic stain in a more marked manner than in health. Within the protoplasm of these cells a faint mucin reaction is sometimes obtained, but in an overwhelming majority of instances this substance is not found within them; this condition is very unusual, as in almost all of the so-called catarrhal inflammations the amount of mucin is greatly increased, but in this instance the quantity is actually much less than in health. Those cells that still remain attached to the basement membranes in the necks of the crypts are unusually swollen, and their free ends often appear ragged, showing beyond doubt that necrotic changes have already begun within them; these cells, however, stain in about the usual way, and, like those that have desquamated, show much less than the normal amount of mucin within their protoplasm. The lumina of the crypts toward their free ends are usually decreased in size on account of the swelling in the intervening connective tissue. The cells that line the lower portions and bases of the crypts show practically no alteration. The only observable change is a disposition to desquamate to a limited extent, and the amount of mucin that is present within them is certainly somewhat less than is usually seen in the normal cells. This diminished mucin formation is likewise evidenced by the fact that very small quantities only of this substance, and in many instances none at all, are found within the lumina of the glands. The lymph node crypts show practically no alteration.

The basement membranes show no change.

The free surface of the tissues intervening between the crypts is covered by finely granular material in which there are many bacteria; these masses of granular debris evidently represent the

necrotic cells and tissues that originally formed the outermost structures in the diseased regions. This granular material stains with acid dyes, as a rule, but there are many particles that take the basic stain with more or less intensity. In many situations there are also found considerable masses of blood mixed with this granular detritus; the red blood cells in these masses of blood are usually swollen, irregular in form, and in many instances have partially disintegrated. Polymorphonuclear leucocytes in varying stages of disintegration always occur mixed with the red blood cells, and frequently lie embedded in the masses of granular debris in situations where there is no blood. Here and there these necrotic changes in the tissues extend downward quite deeply, involving in some instances as much as the outer half of the mucosa. Under these circumstances all of the tissues in the affected area are practically destroyed, the crypts are no longer recognizable, and the intervening connective structures have lost all resemblance to the tissues normally found in these situations. The changes that are present lower down in every way resemble those that have been described as occurring where the necrotic process only involves the surface of the mucosa. Lower down the tissues are greatly swollen and frequently contain ecchymotic areas. The fibrils of both the elastic and collagenous tissue appear to be swollen, and their outlines are ill-defined; they do not react to their specific stains in the normal way. Lying between the fibrils of connective tissue there are numerous cells. These consist, for the most part, of lymphoid cells and large, finely developed plasma cells, but intermingled with them there are a few connective tissue cells and a very small number of mucinoblasts. In certain situations the tissues contain great numbers of polymorphonuclear leucocytes, and where they are present they so largely predominate that they constitute by far the greatest number of cells in the affected area, though there are always found a few lymphoid and plasma cells intermingled with them. In these situations there are many widely dilated bloodvessels, filled with blood, and the tissues are even much more swollen than in the other parts of the mucosa. In some instances this process has gone on to such a degree that the crypts have been almost squeezed out of existence as a result,

and appear merely as columns of cells between the swollen connective tissues. Although carefully examined for, no bacteria were found in these situations. In those parts of the mucosa where the leucocytic infiltration is not so marked the blood-vessels are not infrequently considerably dilated, but they never show this change to such an extent as is seen where the polymorphonuclear white blood cells predominate. Here the change becomes gradually less marked as the bases of the crypts are approached, and in many instances no alteration at all is found in the deepest portion of the mucosa. It is noteworthy, however, that in addition to a slight degree of swelling of the tissue, which may or may not be present, there is a decided diminution in the number of mucinoblasts, and there are generally present quite a number of lymphoid and plasma cells. Where the leucocytes predominate the deeper interstitial structures of the mucosa are always considerably altered; the tissues are swollen, are often quite granular, and the bloodvessels are usually distinctly dilated and are filled with blood. This change does not, however, extend beneath the muscularis mucosæ.

The muscularis mucosæ shows but little alteration, the only apparent change being that there are present between the fibrils quite a number of plasma cells and some lymphoid cells. The muscular tissue and the elastic tissue network of this coat show no alteration.

The submucosa is but little affected, the most marked changes being an unusual degree of dilatation of the veins and presence of quite a number of plasma cells, and lymphoid cells just beneath the muscularis mucosæ. The endothelial cells lining some of the smaller arteries are swollen, and in some instances have desquamated from their basement membranes. In some of the lymphatics there are small collections of fibrin. This coat is somewhat swollen.

No changes are present in the muscular or serous coats.

## EXPERIMENT II. Duration, twenty days.

On October 18, 1900, 1 gm. of calomel was given to a dog weighing 11 kg.; the drug was mixed with the animal's food,

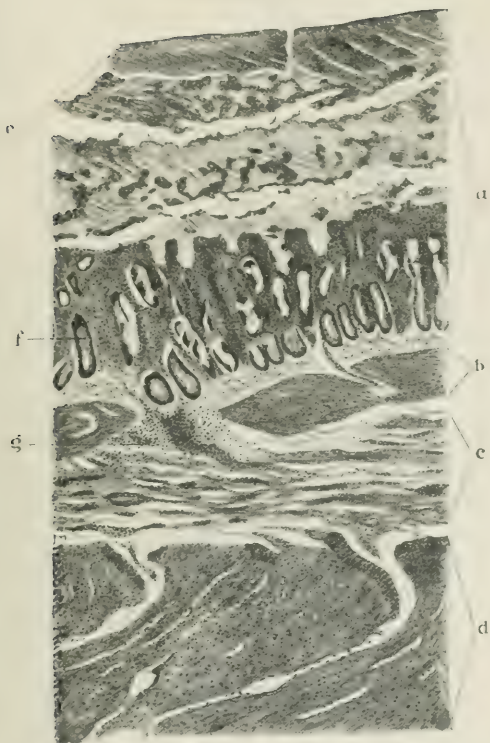
and on the first occasion the entire dose was taken. After this a like amount of calomel was each day mixed with his food, but in most instances only a small quantity of this was actually ingested, as he evidently detected the presence of the chemical and ate very sparingly. After taking the food containing the calomel vomiting usually occurred, but notwithstanding this, at the end of a week the animal was in good spirits and showed no ill effects from the treatment further than that the discharges from the bowels were blood-stained and contained considerable quantities of mucus. A few days later the dog appeared somewhat emaciated, and after this scarcely ate any food at all. During the last week of the animal's life only a very small amount of the calomel was taken. During this period the dog daily grew thinner, became very weak, and showed every evidence of illness. He died during the night of November 7th, twenty days after the initial dose of the drug was given.

On post-mortem examination the stomach and small intestine were found entirely normal, but the lower bowel was empty and its mucous surface showed considerable alteration. The lower margin of the ileocecal valve was of an almost black color and appeared to be superficially ulcerated. The remaining part of the large intestine was free from actual ulceration, but the mucosa was greatly reddened. This redness is greatest on the tops of the rugae. The mucosa of the appendix was also swollen and quite red.

On microscopic examination extensive alterations are found in the mucosa of the intestines; these changes affect all parts of the intestine nearly alike, the region around the ileocecal valve showing but little more change than the tissues in other parts of the bowel. The epithelial cells of the surface of the intestine and of the crypts have in a large measure desquamated, and secondary changes of a pronounced kind are present in the interstitial tissues lying between the glands.

Lying on the free surface of the mucosa there are very generally present masses of mucus, intermingled with which is a granular debris consisting of disintegrating cells and multitudes of bacteria. The necrotic cells that lie in these masses are evidently largely composed of the eroded surface epithelium of the gut, since

PLATE XIV.



Specimen was taken from the upper portion of the large intestine of a dog that had received daily small doses of calomel by the mouth for twenty days before death occurred. The tissues were fixed in Bensley's solution and stained by the method of Van Gieson. Beck  $\frac{1}{4}$  inch, Oc. 1 inch. *a*. Mucosa, the surface of which is necrotic (*a*), and in the deeper portions the epithelial cells of the crypts exhibit catarrhal changes (*e*), and in the intervening tissues new formation of fibrous tissue is going on, and there are present many lymphoid and plasma cells. *b*. Muscularis-mucosae, which is interrupted at (*g*) by the edge of a lymph node. *c*. Submucosa. *d*. Circular muscular layer. The longitudinal muscular layer is not included in the drawing. (Exp. II.)





this layer of cells is universally absent. Necrosis of the upper portions of the crypts and of the intervening tissues is present in some situations. The mouths and necks of Lieberkuehn's crypts show at all points marked catarrhal alteration; the epithelial cells have almost entirely shed off from their basement membranes, are exceedingly irregular in form, in many instances swollen, and their nuclei no longer react to basic dyes; these desquamated cells lie together in masses in the lumina of the crypts from which they come, and in not an inconsiderable proportion of instances have entirely broken up, and there remains only a granular débris representing them. Mucin is present in considerable quantities both within the epithelial cells in these situations and lying loosely in the lumina of the crypts. Lower down in the bodies of the glands the epithelial cells show less extensive change, though at no point do they appear entirely normal. Even here they have in some instances desquamated, and very generally show traces of mucin within their protoplasm. Even those cells that have not shed off from their basement membranes are more or less granular, and are frequently swollen to such an extent that the lumina of the crypts in which they lie are in a large degree obliterated. Mitotic figures are numerous in all parts of the crypts, but are especially common toward the bases of these glands.

The basement membranes of the crypts are practically unaltered.

The tissues intervening between the crypts are greatly increased in amount, and show along the free surface of the mucosa most pronounced necrotic change; in some instances, as has been before remarked, these structures have been eroded away for a considerable distance down into the mucosa. The free surface of these tissues is very ragged and irregular, and consists of greatly swollen masses of collagenous tissue that in its outermost portion is exceedingly granular and stains deeply with acid dyes; lying within these tissues there are a few connective tissue and lymphoid cells, but, on the whole, they contain less than the usual number of cellular elements. The elastic tissue fibres in these situations fail to take the stain, but do not seem to be in a greater degree diseased than the neighboring fibrous structures. A little deeper down the tissues no longer exhibit necrotic changes, but contain

multitudes of most exquisite plasma cells, a great many lymphoid cells, and about the usual number of mucinoblasts. The fibrous structures have greatly increased in these areas, with the effect of diminishing the size of the lumina of the enclosed crypts. The bloodvessels in this region are in many instances considerably dilated, but there is no appearance of leucocytic infiltration into the tissues, nor were hemorrhages in any instance observed. Passing downward into the deeper portion of the mucosa the changes become less and less pronounced, so that around the bases of the crypts there is only here and there an increase in the fibrous tissue structures; however, there are universally present large quantities of lymphoid cells and numerous plasma cells. Mucinoblasts are found in these situations in about the usual numbers.

The muscular and elastic tissues of the muscularis mucosae show no change, but there are found between the fibrils numerous lymphoid cells and not an inconsiderable number of plasma cells.

The submucosa shows no alteration, with the exception that it contains more lymphoid cells than is usual in health, and there are here and there circumscribed collections of plasma cells.

The muscular, subserous, and serous coats show no alteration.

### **Résumé of the Changes Occurring as a Result of Poisoning by Calomel.**

**Acute. (Four and a half days.)** The intestine shows no change further than that there are found scattered over the mucosa minute areas that are somewhat redder than the surrounding surfaces.

The epithelial cells that covered the surface of the bowel, and the mouths and necks of the crypts have universally desquamated. Many of the shed-off cells still remain in the lumina of the crypts, and are swollen, very irregular in form, and contain much less mucin than is usually seen in the cells found in these situations. In some instances there are very small areas in which the outer portions of the glands and the intervening connective tissues have undergone complete necrotic change. Around the edges of these areas, and just beneath the surface of the intestine generally, there

are many dilated bloodvessels filled with blood, and around these there are considerable collections of polymorphonuclear leucocytes. Hemorrhages into the tissues are not uncommon. In addition to the polymorphonuclear leucocytes there are the usual numbers of lymphoid cells, pseudoplasma cells, and a few mucinoblasts. In many instances the interglandular substance is so swollen that the crypts are very much compressed. These changes extend downward through the mucosa, but become less and less until at the edges of the muscularis mucosæ there are practically no alterations.

The deeper coats show no change.

**Chronic. (Twenty days.)** On examination the large intestine was found to be very much inflamed. The mucous surface in the vicinity of the ileocecal valve was almost of a black color, this being evidently due to the formation of the sulphide of mercury. The tissues in this situation have the appearance of superficial ulceration, but this is found in no other part of the intestine. The mucosa of the intestine is almost uniformly reddened. The mucosa of the appendix shows a similar change.

The epithelial cells that covered the surface of the intestine, and the mouths and necks of the crypts, have universally desquamated, and those that line the deeper portions of the glands are swollen and irregular in form, and in some instances have also shed off.

The surface of the interglandular tissue is necrotic. Lower down the tissues are swollen and contain many lymphoid and plasma cells. There has been much new formation of fibrous tissue. These alterations extend no deeper than the mucosa.

## CHAPTER IX.

### EXPERIMENTS TO DETERMINE THE EFFECTS PRODUCED ON THE LARGE INTESTINES OF DOGS AS A RESULT OF THE INJECTION OF TINCTURE OF IODINE.

#### EXPERIMENT I. **Duration, twenty-four hours.**

ON January 15, 1901, 10 c.c. of tincture of iodine (U. S. P.) were injected into the large intestine of a dog. Twenty-four hours later the animal was killed with chloroform, and an autopsy was at once made. The lower half of the large intestine contained no fecal matter, and the mucosa in this portion of the gut was decidedly reddened. The transverse rugæ were quite numerous, but the mucous membrane covering these elevations was no redder than that upon the surrounding surfaces.

On microscopic examination the surface layer of epithelial cells that normally covered the mucosa is found entirely absent, and the tissues that immediately underlay these cells, as well as some of the epithelial cells that covered the edges of the mouths of the crypts, have likewise become necrotic and sloughed away. It is, however, noteworthy that catarrhal changes are nowhere observable in any of the cells that still lie in their normal positions in any of the parts of Lieberkuehn's crypts, this being true even of the cells at the margins of the lesions just referred to. Notwithstanding that catarrhal changes are nowhere found, it is of considerable interest to note that mucin is entirely absent from the cells of the crypts that lie in the regions most affected, nor is that substance ever present in the lumina of the crypts. The basement membranes upon which the epithelial cells lie are entirely normal.

The most pronounced changes found in the intestine are those that occur in the interglandular substance of the mucosa. In these areas the bloodvessels are enormously dilated and are filled with blood; in many instances they have ruptured, and when

this has occurred quantities of blood are found effused into the neighboring tissues. In addition to the free red blood cells there are a considerable number of lymphoid cells, a great many plasma cells, a few mucinoblasts, and polymorphonuclear leucocytes. It is of some interest to note that those mucinoblasts that still remain in the parts are small and even more irregular in shape than usual, and in the liquids immediately surrounding them there is a zone in which the mucin reaction is distinctly obtained; it would thus appear that the mucin was undergoing solution at the time the animal was killed. It should, perhaps, be stated that the stain with which the above reaction was obtained was carbol toluidin-blue and not Unna's alkaline methylene-blue, which, on account of the fact that it dissolves out the mucin, frequently gives the appearances around mucinoblasts that have just been described. In addition to the cellular elements that are so numerous present in the interspaces of the tissues there are many small cellular fragments and a considerable quantity of fluids. The pre-existing collagenous and elastic tissues normally found in the parts present no perceptible alterations. It is, of course, obvious that much distention of the interglandular substances must have resulted from the various pathologic alterations that have been described, and as a result the crypts of Lieberkuehn have been compressed to such an extent that oftentimes they are scarcely more than one-half of their normal diameter. The changes above recorded are, as a rule, much more pronounced in the outer half of the mucosa, but always extend to a greater or less extent down to the muscularis mucosæ.

The only changes observable in the muscularis mucosæ are that there are here and there small collections of lymphoid cells, intermingled with which there are commonly a few polymorphonuclear leucocytes.

The layer of the submucosa lying next to the muscularis mucosæ also shows here and there small collections of lymphoid cells, and a few polymorphonuclear leucocytes are in addition occasionally found. The bloodvessels in this situation are also rather unusually prominent, seem somewhat dilated, and are always filled with blood. No further changes are found in this coat.

The other coats of the intestine are normal.

EXPERIMENT II. **Duration, eighteen days.**

On January 15, 1901, 10 c.c. of tincture of iodine (U. S. P.) were injected into the rectum of a medium-sized dog. On the following day the animal appeared weak and was observed to pass considerable quantities of bloody mucus. The injections were repeated on the 18th, 21st, 24th, 27th, and 30th of January, but for the reason that the animal was so decidedly affected by the first dose, only 5 c.c. of the iodine solution were afterwards given. During the period when the dog was receiving these injections he became rapidly emaciated and suffered continually with diarrhoea. On the morning of February 2, 1901, eighteen days after the first injection was given, the animal was found in a dying condition; chloroform was administered until death was produced, and an autopsy was at once made. The large bowel was almost empty, but there were present here and there small quantities of semi-liquid fecal matter of a dark brown, almost black color. Except just at the upper end of the gut, the entire intestine was thrown into numerous transverse folds; the mucosa was very pale, resembling in color ordinary hyaline cartilage very closely.

On microscopic examination the surface layer of epithelium is found for the greater part absent in the affected regions, but beginning at the mouths of the crypts the cells that line these structures appear entirely normal, with the exception only that in no part of the glands do they show mucin formation. It may be remarked, however, that mitotic figures are decidedly more frequent in the epithelial cells of the glands than is usual. On account of the pressure that is produced as a result of the presence of newly-formed fibrous tissue in the interglandular substance the lumina of the crypts have much diminished in size, and the glands from basement membrane to basement membrane often measures no more than  $30\mu$ . The elastic tissue basement membranes of the crypts show no alterations.

Notwithstanding that the surface layer of Lieberkuehn's crypts appear practically normal, the lymph node glands show very decided alterations. These changes are almost entirely confined to

the bodies and basal portions of these structures, for the cells lining their necks and mouths present practically no alterations. In truth it may be stated that almost without exception the structures composing the deeper portions of the crypts have undergone necrotic change and have nearly or entirely disappeared. Filling up the area originally occupied by the glands there are numerous polymorphonuclear leucocytes, intermingled with which are a few lymphoid cells, an occasional swollen epithelial cell, and a small quantity of granular débris. The tissues of the surrounding lymph nodes contain in all instances quantities of newly-formed fibrous tissue, intermingled with the fibres of which there are numerous plasma cells, quite a number of lymphoid cells, and a few polymorphonuclear leucocytes.

In those situations where the epithelial cells have been eroded from the surface of the interglandular tissues, the structures composing them, even at their edges, present no obvious alterations; this is apparently due to the fact that in these situations there is being produced quantities of white fibrous tissue, and that this substance and the cells generating it compose the surface layers of the tissues in the diseased regions.

Deeper down between the glands great quantities of fibrous tissue is also being produced, this substance already having so increased in the diseased areas that the crypts, as has been before stated, are greatly compressed. In addition to the newly-formed white fibrous tissue, plasma cells are abundantly found, and their transformation into the so-called fibroblasts and the formation of collagenous tissue around their borders is most clearly and beautifully shown. The lymphoid cells that are always present in these situations in health have practically all been transformed into plasma cells. Here and there is found a small, ill-formed mucinoblast; these cells are much less abundant than in health. The bloodvessels in the diseased areas are sometimes slightly dilated; but we do not find here that degree of vascular change that was so pronounced in the acute changes resulting from the application of iodine. As the basal portions of the glands are approached the alterations become gradually less and less pronounced, and in the deepest portions of the mucosa newly-formed fibrous tissue is never present, though plasma cells are quite



numerous. Here and there are found quite a number of lymphoid cells and a very few mucinoblasts.

The muscularis mucosæ presents no obvious alteration.

The layer of the submucosa immediately beneath the muscularis mucosæ contains numerous plasma cells, intermingled with which there are quite a number of lymphoid cells and here and there a few polymorphonuclear leucocytes. In this region there has evidently occurred a new formation of collagenous tissue to a considerable degree, the tissues being much denser than normal, and in many instances plasma cells may be seen in the process of producing this substance. The bloodvessels in the same area are somewhat more numerous and appear larger than is normally the case. Mucinoblasts are occasionally present in this layer, but are by no means so numerous as in health. Changes of a similar kind extend throughout the tissues of the submucosa, but the deeper portions do not exhibit alterations to the same degree as is found more superficially.

The other coats of the intestine present no alteration.

### Résumé of the Changes in the Tissues Resulting from the Injection of Tincture of Iodine.

Where the changes are *acute*, erosion of the epithelium occurs, but the cells lining Lieberkuehn's crypts present no alterations other than that mucin formation is much diminished or entirely ceases.

The interglandular structures of the more superficial portions of the mucosa are greatly swollen as a result of the presence of quantities of effused blood, enormous dilatation of the bloodvessels, and many plasma cells; mucinoblasts are diminished in number, and when present are ill-formed and much smaller than usual.

In *chronic* poisoning by iodine the changes in the epithelial structures of the mucosa are essentially similar to those that are seen in the acute conditions, with the exception that there have occurred catarrhal changes in the lymph node glands, and around them there is usually a condition that closely resembles



suppuration ; surrounding the diseased area there is much newly-formed fibrous tissue.

The interglandular tissues of the surface crypts show the formation of great quantities of newly-formed white fibrous tissue. Plasma cells are in these situations numerous, and their transformation into the so-called fibroblasts and the formation of collagenous tissue around them is most exquisitely shown. The blood-vessels are but little dilated. Mucinoblasts are rarely found. In the more superficial portions of the submucosa white fibrous tissue is being formed to a considerable extent, and here again the relation of plasma cells to the production of collagenous tissue is most clear.











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